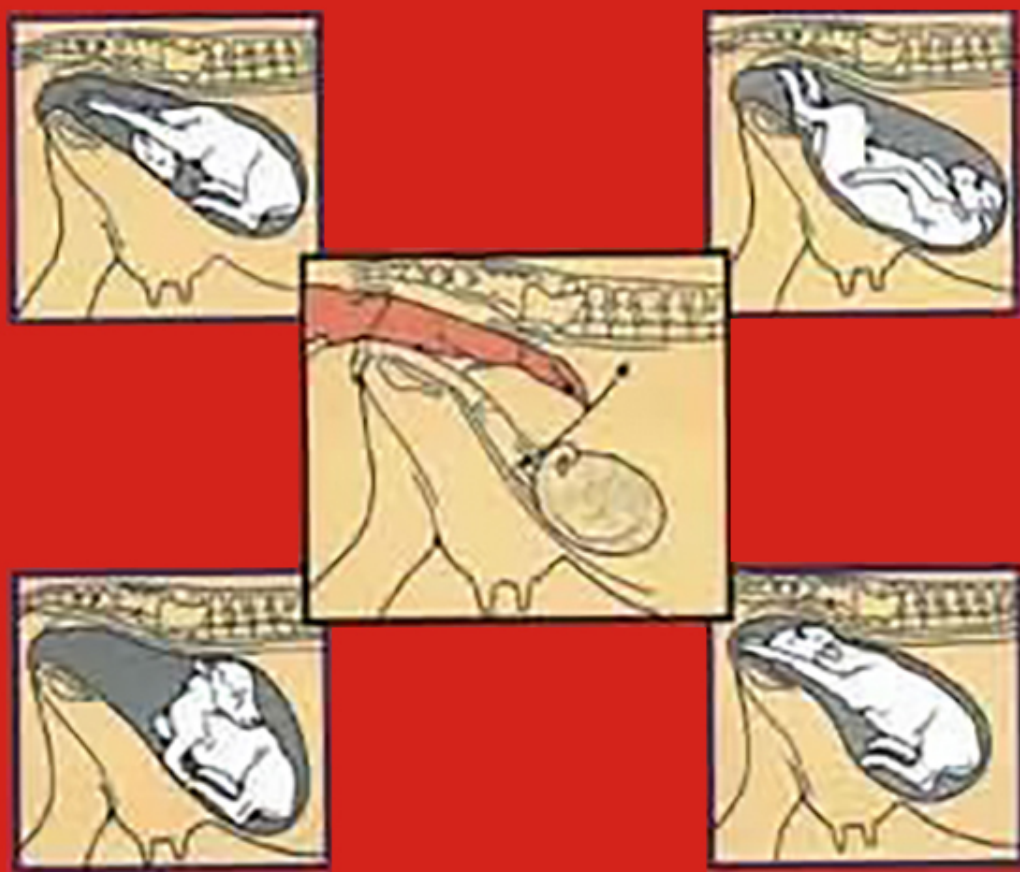


VETERINARY OBSTETRICS AND GENITAL DISEASES

THIRD EDITION



STEPHEN J. ROBERTS

VETERINARY OBSTETRICS
AND
GENITAL DISEASES
(THERIOGENOLOGY)

VETERINARY OBSTETRICS AND GENITAL DISEASES (THERIOGENOLOGY)*

by

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*(Term proposed by D. Bartlett and others to indicate all aspects of *veterinary* obstetrics, genital diseases and animal reproduction; "therio" = animal or beast and "gen" = coming into being from Greek medical terminology.)

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Dedicated
to
Beejay

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PREFACE

This third edition has engendered in the author a sense of enormous humility and gratitude. Humility in the realization of the great efforts, expenditures, honesty, study and research of innumerable persons who have contributed to all aspects of this broad interdisciplinary subject of reproduction in animals and man. The number and breadth of the selected references reviewed by the author has been an enriching experience and attests to the willingness of those in this field to share and advance the accumulated and new knowledge. As one of my former professors remarked, "Everything I know has been built on research and knowledge of other persons."

This current field of reproduction has a strong heritage going back over 60 years to studies by W. L. Williams, Nils Lagerlof, E. C. Amoroso, F. Benesch, C. G. Hartman, A. S. Parkes and L. E. Casida. In more recent times the tradition of excellence has been carried on by: K. McEntee, M. G. Fincher, R. Zemjanis, Wm. Hansel, H. H. Cole, P. T. Cupps, L. E. McDonald, O. J. Ginther, G. H. Arthur, M. Vandeplassche, J. Hughes, W. B. Pickett, R. H. Foote, W. R. Allen, D. A. Morrow, E. S. E. Hafez, L. Ball, E. L. Squires, M. Drost, and many others to whom we all owe a sincere and continuing debt.

In this third edition the author is pleased to be able to include the reviews and insights of his colleagues, Donald H. Lein, R. H. Foote and M. Drost who have contributed Chapters XVII, XIX and XX on Infertility in Bitches and Queens, Artificial Insemination, and Embryo Transfer, respectively. With my retirement from Cornell University in 1972 and entering a busy general practice with my brother James F. Roberts in Woodstock, Vermont, it was impossible to keep fully abreast with the progress and literature within these three fields so graciously and competently reviewed by these contributing authors.

For the rest of the text the author takes full responsibility for its shortcomings in English grammar and exposition. His primary concern was the organizing, documenting and abstracting of new and pertinent knowledge and fitting it into the framework of his first and second editions. "The printed word is not the truth nailed down,

it is the author."* At the suggestion of my professional colleagues, the author has removed nearly all individual names of researchers and reviewers from the text and replaced them with reference numbers. He hopes this will improve the readability of the text without detracting from the importance of the individuals' contribution.

This third edition was a challenge and a goal that nearly overwhelmed the author by the enormous increase in published material. Fortunately his health and eyes have remained excellent due to his wife's food, ministrations and understanding that have enabled him to spend the many hours of necessary reading, filing and writing.

The author has purposely not tried to simplify, eliminate controversial material, or omit any phase of the subject that concerns itself with veterinary obstetrics or genital diseases of domestic animals. This book was written for veterinary undergraduates and those practitioners who are still students. The layman was not considered, as to do so would make the text less satisfactory for its intended readers. The author has stressed diagnosis and physiology throughout the text because he feels these phases are of greatest concern for veterinarians. An accurate diagnosis often requires an extensive knowledge of the field and of all the possible conditions that may be responsible for certain symptoms. As Bertillon, the famous French detective said, "One can only see what one observes, and one observes only things which are already in the mind." Students might prefer a streamlining of information such as befits a core course. But each case in practice is different and a breadth of specific knowledge, skill and the art of its applications are essential.

This text would not have been possible without access over the years to the outstanding Flower Veterinary Library at Cornell and its skilled, pleasant and cooperative librarians. The author must also extend his appreciation to Dr. Kenneth McEntee, his respected colleague, who was a source of knowledge in reproductive pathology,

* From Fischer, M. H., Professor of Physiology, University of Cincinnati.

and also a source of illustrative material both of which were freely offered. My brother Jim and his wife, Dot, must be thanked for graciously and at a sacrifice allowing him extended "sabbatics" to work uninterruptedly at the New York State College of Veterinary Medicine at Cornell in the winters of 1981-1982 and 1982-1983. Ms. Joyce Reyna deserves grateful recognition for her secretarial services and help, as does his printer of the past 30 years, Edwards Bros., Inc., Ann Arbor, Michigan.

My past 10 years in veterinary practice in Woodstock, Vermont, has been very rewarding in personal satisfaction and in the realization of the many facets necessary to provide a needed service "out where the action is." It has given me great moments of pleasure and gratifi-

cation to combine my "ivory tower" knowledge and associations with practical on the farm and in the office transmittal and application of this knowledge. This interface is the ultimate area where veterinary knowledge serves animals and man. I am grateful to have lived and worked in the veterinary profession during what may have been the "golden age" of veterinary medicine and scientific progress. It has been inspiring, fascinating and challenging to keep abreast of many of these advances. However it has also provided rewarding satisfaction and opportunities for service.

Woodstock, Vermont
January, 1986

S. J. Roberts

Part I

INTRODUCTION

Veterinary obstetrics has in the past been defined as that branch of surgery dealing with the oversight of the female animal during pregnancy and parturition. However, with our increased knowledge of genital diseases of female and male animals, the study of veterinary obstetrics has expanded to include the latter highly important field. The livestock industry depends upon reproduction. Any disease or pathological condition causing sterility or infertility in our domestic animals, whether it be a sporadic or enzootic condition, must be the concern of veterinary practitioners. The recent introduction and rapid growth of artificial insemination, and its inherent problems, require the modern veterinarian, especially in cattle practice, to be well acquainted with this field of obstetrics. The fields of reproductive physiology, endocrinology, immunology, nutrition, genetics, embryology, teratology, anatomy, virology, bacteriology, pathology, surgery, and medicine, all supply important necessary links in our chain of obstetrical knowledge. In the broad interdisciplinary field of veterinary obstetrics and genital diseases, as in any clinical field of study, the advances made in the basic sciences must be

studied, considered, and applied.

For the veterinarian entering practice the importance of this field of obstetrical and genital disease cannot be overestimated. The figures from the large New York State Veterinary College Ambulatory Clinic, in which 85 to 90 percent of the animals treated are dairy cattle, show that about 25 to 30 percent of the cases treated were obstetrical or dealt with the reproductive system. These include such common conditions as dystocia, retained placenta, pregnancy examination, sterility examination and treatment, abortion, metritis, blood testing, vaccinating for brucellosis and other abortion diseases and the treatment of many other genital conditions. From a purely business viewpoint, the volume of obstetrical work in a large animal or small animal practice is considerable. One must realize that the average layman or farmer places an undue amount of importance and significance on the successful handling of obstetrical cases and breeding problems. The young or inexperienced veterinarian may make or ruin his chances for success with a certain farmer or in a certain territory by the way in which he handles a single obstetrical case or problem.

Chapter I

FEMALE GENITAL ANATOMY AND EMBRYOLOGY

The bony and ligamentous structures comprising the pelvis are of particular interest in obstetrics. The bony pelvis is composed of the **sacrum**, the first to third **caudal vertebrae** and the two **ossa coxarum**, each formed by the ilium, ischium and pubis.

The **sacrum** is composed of five fused vertebrae in the cow. It is somewhat triangular in form with the base articulating cranially with the last lumbar vertebra and caudally with the first caudal vertebra. The ventral face of the sacrum is smooth and concave. The dorsal surface exhibits the sacral spine. The wing of the sacrum articulates or fuses with the ilium laterally as the sacroiliac joint. In older animals the first caudal vertebra may fuse with the sacrum in the horse, cow and pig.

The **ilium** is irregularly triangular in shape. The broad, flat, dorsal part of the ilium is called the wing. The medial portion of the wing is called the tuber sacrale and its ventral medial aspect articulates with the sacrum. The external portion of the wing of the ilium is called the tuber coxae, hip bone, or "hook" bone. Dorsally the wing of the ilium in the horse, cow, sheep and pig is concave, providing attachment for the gluteal and back muscles. Ventrally the wing is convex. In the dog and cat the wing of the ilium is rotated laterally so it lies nearly parallel to spinal column. The narrow, ventral part of the ilium is called the body. This bone fuses ventrally with the ischium and pubis at the acetabulum. Its medial or pelvic surface is smooth and is grooved for the obturator vessels and nerve.

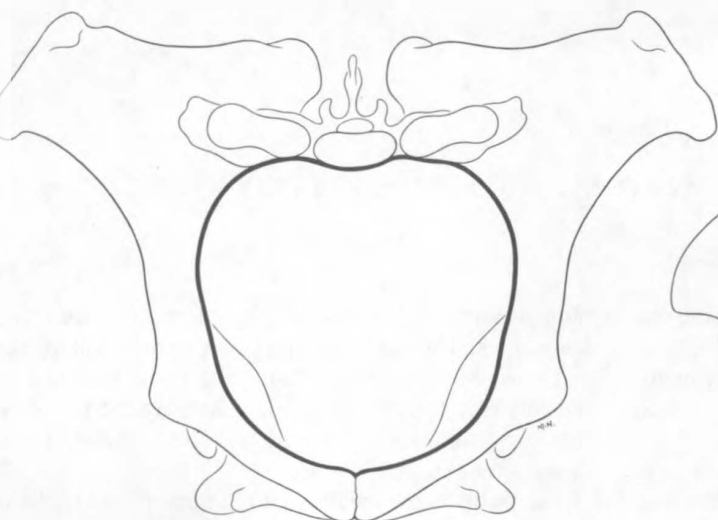
The **ischium** forms the caudal part of the ventral floor of the pelvis. Its dorsal surface is smooth and rather concave. The caudal border of the ischium slopes inward and forward to join with the opposite ischium to form the ischiatic arch. The caudal lateral portion of these bones is called the ischiatic tuberosity or "pin" bone. The ischiatic tuberosity in the pig is largely cartilaginous in nature and the symphysis does not undergo complete ankylosis until 6 or 7 years of age. The cranial border of the ischium forms the caudal margin of the obturator foramen. Dorsally the ischium bears the ischiatic spine, cranial and caudal to which are the greater and lesser sciatic notches respectively. These notches become fo-

ramina when the sacrosiatic ligament completes their boundaries. The ischiatic spines are prominent in the sow and cow. Medially the ischium and pubis fuse to form the pelvic symphysis. In the cow and ewe the portion of the pelvic floor formed by the two ischia is deeply concave from side to side.

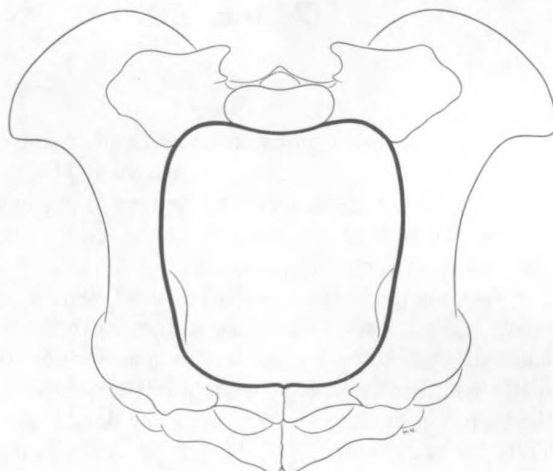
The **pubis** is the smallest of the three bones of the os coxae and forms the cranial portion of the pelvic floor. The dorsal or pelvic surface is smooth and usually concave in females, while in males it may be convex. Occasionally in the young cow a sharp tuberosity projecting into the pelvic canal is present on the cranial portion of the pubic symphysis. This prominence may rarely cause contusion or even laceration of the birth canal during a difficult birth. The cranial medial border of the pubic bone provides attachment for the prepubic tendon. The caudal border forms the cranial border of the obturator foramen.

The **acetabulum** is formed by the fusion of the ilium, ischium, and pubis. These bones form a cotyloid cavity lodging the head of the femur. The acetabulum consists of articular and non-articular portions. The acetabular notch is made into a foramen by the transverse ligament and transmits the accessory ligament to the head of the femur in the horse. The ligament of the femoral head is a short, strong band between the head of the femur and the acetabulum.

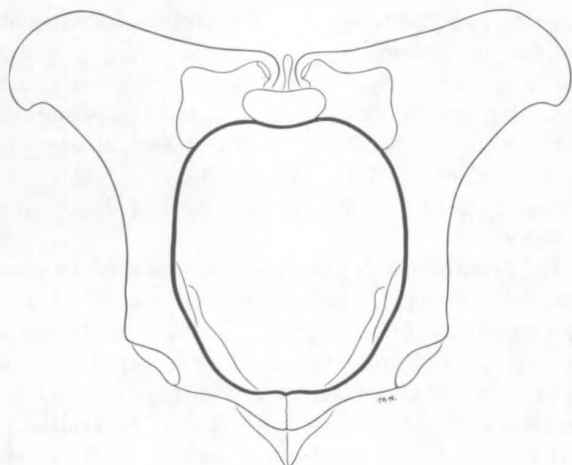
There are three, single or paired, **pelvic ligaments** that maintain the relationship of the pelvis to the spinal column. (1) **The dorsal and lateral sacroiliac ligaments**, which are attached to the medial wing of the ilium and lateral portion of the sacrum and the summits of the sacral spines. This articulation is very firm and rigid and is further maintained and supported by the sacrosiatic ligament and prepubic tendon. (2) **The sacrosiatic ligament** is an extensive quadrilateral aponeurosis that completes the lateral wall of the pelvic cavity. The ligament extends from the lateral border of the sacrum and the transverse processes of the first two caudal vertebrae to the ischiatic spine and tuber ischii. It furnishes attachment for the large gluteal muscles and the vulva. In the dog this ligament, called the sacrotuberous ligament,



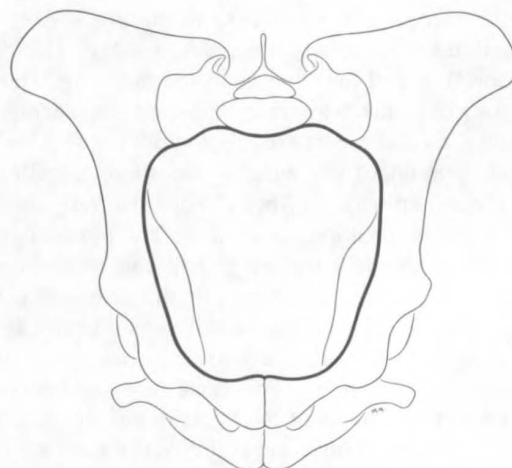
Pelvis of Mare



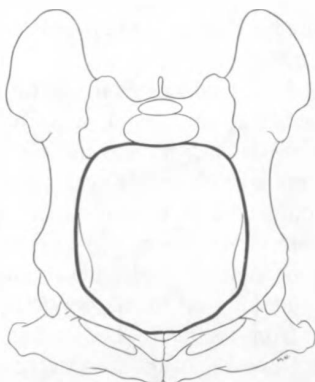
Pelvis of Sow



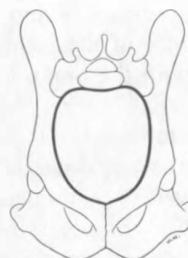
Pelvis of Cow



Pelvis of Ewe



Pelvis of Bitch



Pelvis of Queen

Figure 1. Pelves of the domestic animals.

is a narrow strong band extending from the caudal part of the lateral margin of the sacrum to the tuber ischii. (3) The **prepubic tendon** is essentially the tendon of insertion of the rectus abdominis muscle. It is attached strongly to the cranial border of the pubic bones.

The pelvic cavity is somewhat cone-shaped, with the base of the cone located cranially. This base is formed by the bony pelvis. The pelvic inlet is roughly oval in shape in all species, with the largest diameter being sacro-pubic. The size of the pelvic inlet varies greatly within a species due to breed, age and size. The sow and cow have the most elliptical pelvic inlets; while the mare and some dogs have nearly round inlets. (See Figure 1) The approximate diameters of pelves of domestic animals are given in Table 1.

Table 1. Approximate Diameters of the Female Bony Pelvis

Species	Sacro-pubic cm	Iliac cm
Mare	20.3–25.4	19.0–24.1
Cow	19.0–24.1	14.6–19.0
Sheep	7.6–10.8	5.7– 8.9
Sow	9.5–15.2	6.3–10.2
Bitch	3.3– 6.3	2.8– 5.7

In our larger domestic animals the cross section of the fetal chest or hips may be greater in diameter than the maternal pelvic inlet but birth is possible by the displacement and realigning of the fetal parts at the time of parturition. The caudal portion of the pelvic cavity is smaller than the cranial portion formed by the bony pelvis but the caudal portion at the time of parturition dilates markedly to allow the passage of the fetus. This ability to dilate is brought about by the relaxation of the pelvic ligaments, especially the sacrosciatic ligament. This relaxation in the cow is an obvious indication of approaching parturition.

The pelvis of the male domestic animal differs from the female in a number of definite points. The diameter of the pelvic inlet is smaller in the male and the ischiatic arch is usually narrower. The pelvic cavity is smaller and less roomy than in the female. The obturator foramen is smaller in the male. The cranial floor of the pelvis is more apt to be convex in the male while it is usually concave in the female. The bones of the pelvis are thicker and heavier in the male. The pelvis of the male castrated at an early age resembles that of the female. These differences are most noticeable in the larger domestic animals.

The comparative differences, other than size, between

the pelves of the various animals should be noted. In the mare the transverse or iliac and sacro-pubic diameters are nearly alike, making the pelvic inlet almost spherical. The coxal tuberosities are large and prominent and the wings of the ilia are nearly perpendicular to the long axis of the body. In the cow the ischial tuberosities are prominent and high. The ilia and coxal tuberosities are smaller than in the mare. The pelvic inlet is more elliptical than in the mare. The pelvis of the ewe is similar to the cow in the shape of the inlet but the wings of the ilia are more nearly parallel to each other and the tubera ischii are relatively much smaller. In the sow the pelvic inlet is long and narrow. The wings of the ilia are not prominent and large, as in the cow and mare. The symphysis pubis in the sow is thicker and does not undergo complete ankylosis. The tubera ischii are not completely ossified. In the bitch the wings of the ilia are small and nearly parallel with the median plane. The ischium has a twisted appearance, since the caudal part is nearly horizontal. The pelvis of the queen is similar to that of the bitch but has a relatively larger obturator foramen.

The **coxo-femoral articulation** is a ball-and-socket joint with the head of the femur fitting into the acetabular fossa made deeper by the cotyloid ligament. This is a fibrous band circling the acetabular fossa. The transverse acetabular ligament crosses the acetabular notch. The ligament of the femoral head extends from the subpubic groove in the acetabulum to the head of the femur and is intra-articular. In occasional cases this ligament may be small or absent.

The increased frequency of hip joint or coxo-femoral dislocation in the cow is due to the shallowness of the acetabulum, lack of bulky muscle around the joint, the small, or occasionally absent, ligament of the femoral head, absence of the accessory ligament present in the mare, the awkward gait, excessive relaxation of the pelvic ligaments in advanced pregnancy and with cystic ovaries, and the large size and weight of the abdomen in advanced pregnancy, twin pregnancy and hydrops of the fetal membranes.

The Ovaries and Female Genital Tract

The generative organs of the female consist of the ovaries and the tubular portion of the reproductive tract including the oviducts or uterine tubes, uterus, cervix and the cranial portion of the vagina arising from the primitive Mullerian or paramesonephric ducts. The vulva, vestibule and the caudal portion of the vagina develop from the urogenital sinus.

The **ovaries** consist of a stroma or network of con-

connective tissue and blood vessels surrounded by a covering of peritoneum except at the attached border or hilus where the vessels and nerves enter. Within the ovary are interstitial cells, primitive ova, developing or secondary ova or follicles, maturing or mature Graafian follicles, atretic or degenerating follicles, and developing, mature or degenerating corpora lutea. The ovary is supported and attached by the portion of broad ligament called the mesovarium dorsally and laterally and by the proper ligament of the ovary medially. Ovaries increase in size as the animal becomes older. The blood supply to the ovary is from the ovarian artery. Varying degrees of anastomoses between the ovarian and uterine arteries as well as the close apposition of the tortuous ovarian artery and the utero-ovarian vein in most domestic animals, except the mare, result in a local venoarterial pathway for prostaglandins from the endometrium to induce luteolysis.^{2,8} The nerve supply is the autonomic nerves from the ovarian plexus that arises from the renal and aortic plexuses.^{7,12}

In the **cow** the ovaries are oval in shape and vary in size from 1.3 to 5 cm. in length, 1.3 to 3.2 cm. in width and 0.6 to 1.9 cm. in thickness. The right ovary is usually slightly larger than the left, since it is physiologically more active. Ovarian weight varies from 5 to 15 gm. per ovary with the average weight of both ovaries in cattle of all ages being 19.5 gm.⁶ The size of the ovary varies depending upon the structures present either corpora lutea or follicles. The bovine ovaries are located on the cranial border of the broad ligament, occasionally under it, on the ventral lateral floor of the pelvis near, on, or slightly cranial to the pelvic inlet and slightly cranial and lateral to the internal os of the cervix. The pocket formed by the proper ligament of the ovary and the mesovarium is called the ovarian bursa. In the dog the mesosalpinx forms the bursa. The mature Graafian follicle is usually about 1.0 to 2.0 cm. in diameter and smooth, convex, thin-walled, and fluctuates on palpation. The corpus luteum is usually about 1.9 to 3.2 cm. in diameter and may comprise up to three-quarters of the size of the ovary. The corpus luteum of pregnancy and the mature corpus luteum of the estrous cycle weigh from 3 to 9 gms. or an average of 5 to 6.5 gm. Its consistency is liver-like. It is usually, but not always, irregular in outline with a protrusion or crown that may be variable in size, from 0.5 to 1.5 cm. in diameter extending 0.5 to 1.0 cm. above the surface of the ovary. About 3 to 5 days after ovulation the corpus luteum can be recognized by rectal palpation. About three days before the next ovulation the corpus luteum begins to regress in size, gradually atrophies and is replaced by connective tissue, the corpus albicans. The corpus albicans replacing the

corpus luteum of pregnancy is large, 2 to 5 mm., and persists indefinitely. These structures tend to make old cows' ovaries feel quite fibrous and roughened. The position of the ovary in the cow varies with the stage of pregnancy or with the size and contents of the uterus. During pregnancy the ovary tends to be drawn downward and forward into the abdominal cavity. In older, pluriparous cows the ovaries and non-pregnant uterus often lie over the brim of the pelvis on the caudal floor of the abdominal cavity. Usually by the fourth or fifth month of pregnancy the ovaries are drawn forward out of reach of the hand on rectal palpation. (See Figures 2, 3 and 6).

In the **mare** the ovaries are bean-shaped and vary in size from 4 to 8 cm. in length, 3 to 6 cm. in width and 3 to 5 cm. in thickness and weigh 30 to 90 gm. They are suspended in the abdominal cavity by the mesovarium or cranial portion of the broad ligament. The ovaries are 5 to 7.5 cm. dorso-lateral to the uterine horns and joined to them by the proper ligaments. A few or several developing follicles 1.3 to 6.3 cm. in diameter may be present in one or both ovaries. Occasionally follicles may reach a size of 7.5 to 10.0 cm. in which case the ovary is temporarily greatly enlarged. The corpus luteum in the mare is about 2 to 3 cm. in diameter within the substance of the ovary. It can be palpated several days after ovulation as a small protrusion in the region of the ovulation fossa and for about 7 days as a pear-shaped structure, liver-like in consistency. It does not project above the surface of the ovary because of the dense, thick tunica albuginea investing the ovary of the mare. The free border or concave portion of the ovary in the mare is spoken of as the ovulation fossa. (See Figures 4, 5 and 7).

In the **ewe** the ovaries are almond-shaped, about 1.3 to 1.9 cm. long resembling those in the cow.

In the **sow** the ovaries are oval in shape about 4 to 5 cm. long, weighing 3.5 to 12 gm., but in maturity having a mulberry-like appearance due to multiple follicles, and/or corpora lutea. Porcine ovarian follicles are normally about 7 to 8 mm. and corpora lutea about 12 to 15 mm. in diameter. The location of the ovaries in gilts is approximately the same as in the cow. Due to the long broad ligament, the location of the ovaries in the abdominal cavity in older sows is variable. The sow's ovaries are almost completely covered in the ovarian bursae by the mesosalpinx.

In the **bitch** and **queen** the ovaries are oval in shape, 1.0 to 3 cm. in length, 0.7 to 1.25 cm. in width and 0.5 to 0.75 cm. in thickness and firmly fastened just beneath the third and fourth lumbar vertebrae, 1 to 4 cm. caudal to the corresponding kidney. The ovaries are concealed in the ovarian bursae which have a 0.6 to 2.0 cm. slit-

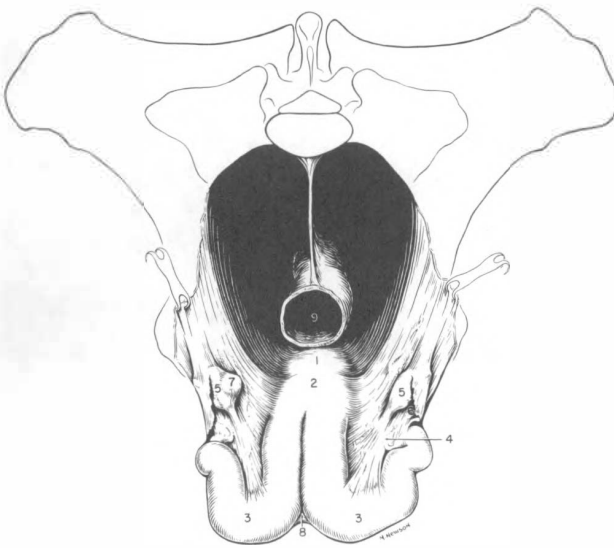


Figure 2. Nonpregnant uterus of the cow, cranial aspect. 1. Cervix, 2. Body of uterus, 3. Horn of uterus, 4. Uterine tube, 5. Ovaries, 6. Ovarian ventricle, 7. Corpus luteum, 8. Intercornual ligament, 9. Rectum.



Figure 3. Uterus of cow, dorsal aspect. 1. Ovarian bursa, 2. Ovary, 3. Corpus luteum, 4. Follicle, 5. Corpus albicans, 6. Uterine tube, 7. Uterine horn, 8. Uterine body, 9. Cervix, 10. Vagina.



Figure 4. Genital tract of the mare. 1. Vulvar lips, 2. Clitoris, 3. Vestibule, 4. Urethral orifice, 5. Vulvovaginal fold, 6. Vagina, 7. Frenulum, 8. Cervix, 9. Body of uterus, 10. Horns of uterus, 11. Mesometrium, 12. Uterine tube in mesosalpinx, 13. Fimbria of uterine tube, 14. Ovary.

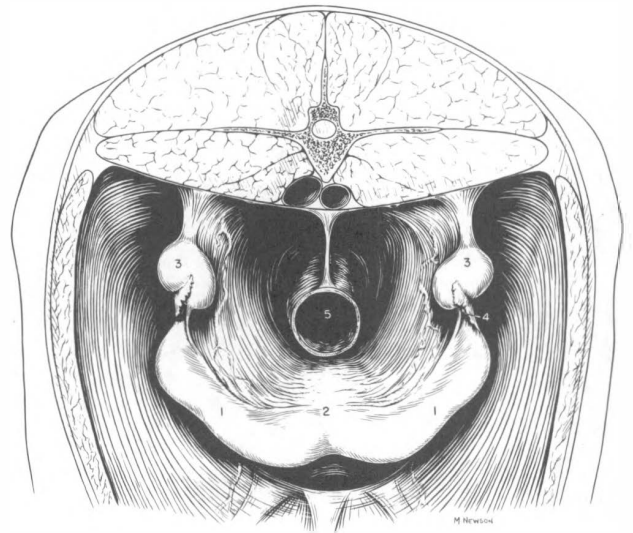


Figure 5. Nonpregnant uterus in the mare. 1. Uterine horns, 2. Uterine body, 3. Ovaries, 4. Uterine tube, 5. Rectum.



Figure 6. Bovine Ovaries—The right ovary contains 2 corpora lutea and an atretic follicle. Left ovary is small since a double ovulation occurred in the right ovary about 6 days ago.

like opening medially.⁵ The wall of the ovarian bursa in the bitch usually contains fat. The ovary in the bitch and queen, like that of the sow may be mulberry-like in appearance due to multiple follicles or corpora lutea. The corpora lutea contain no pigment.

In the queen, the ovaries are similar to the bitch but are suspended more ventrally in the abdominal cavity. The ovarian bursa contains no fat.

The tubular genital tract develops from the primitive paramesonephric (Mullerian) duct system. These primitive ducts, two in number, unite caudally in the region of the vagina, cervix and body of the uterus to form a long tube with various constructions that is modified in structure and function to protect the developing fetus.



Figure 7. Equine Ovary—The corpus luteum is protruding into the ovulation fossa. Note depression over CL due to loss of follicular fluid at the time of ovulation about 48 hours ago.

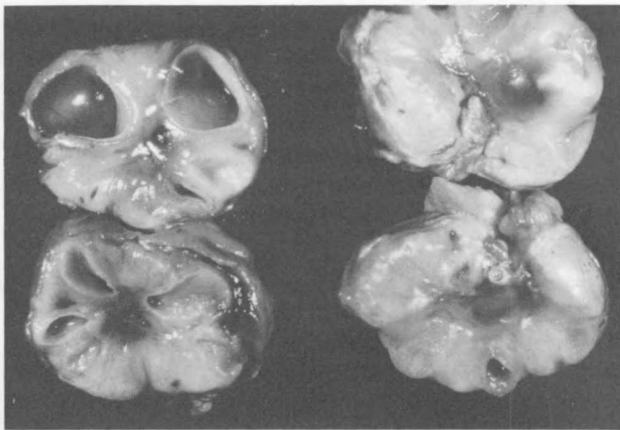


Figure 8. Ovaries of a mare bisected—Note pear-shaped follicles with narrow portion toward the ovulation fossa.

The **uterine tube** or **oviducts** are about 20 to 30 cm. long and about 1.5 to 3.0 mm. in diameter in the mare and cow. They are tortuous, wiry and hard, feeling nearly cartilaginous when rolled between the fingers. They may be imbedded in fat in the mesosalpinx, a portion of the broad ligament supporting the uterine tube. The oviducts or uterine tubes are difficult to palpate on rectal examination. Bimanual vaginal and rectal examination often is of assistance in palpating the uterine tube. Another technique in the cow is to slip several fingers into the ovarian bursa or ventricle and palpate the uterine tube between them and the thumb. The distal or caudal, short segment, 1 to 3 cm. in length, attached to the tip of the uterine horn is called the isthmus; while the major portion of the uterine tube from the isthmus to the infun-



Figure 9. Ovaries of a sow—Note mature corpora lutea and small follicles.

dibulum is called the ampulla. The diameter of the uterine tube at the ovarian end becomes larger, 4 to 8 mm. and the uterine tube becomes funnel-shaped, the infundibulum. From this funnel-shaped end of the uterine tube arises the fimbriated portion of the tube. This has a partial attachment to the lateral side of the ovary and to the proper ligament of the ovary medially. The uterine end of the uterine tube in the bitch and mare opens into the uterine lumen through a small slit on a mound or papilla. In the cow and ewe there is a marked flexure at the transition of the isthmus with the elongated curving end of the uterine horn. The latter has a very narrow lumen. In the sow and bitch the mucosa of the uterine tube projects into the uterine lumen as folds well-supplied with blood.^{10,11} The uterine tube of the sow is 15 to 18 cm. long; that of the bitch and queen is 4 to 9 cm. long and has a slightly tortuous course around nearly the entire circumference of the ovarian bursa. The blood supply of the uterine tube is from the uterine and ovarian arteries. The nerve supply is the same as that of the uterus and ovary.

The **uterus** is a muscular membranous structure designed for the reception of the fertilized ovum, for the nutrition and protection of the fetus, and for the initial stage of its expulsion at parturition. The form of the uterus in animals varies with the degree of fusion of the paramesonephric ducts. The endometrium of the uterus in domestic animals is the only structure that can form sufficient placental attachment to result in normal development of the embryo and fetus. In uniparous animals the placenta lies against the cervix, while in multiparous animals the placenta does not touch the cervix. The muscular coat of the uterus is composed of smooth muscle in circular and longitudinal layers. The uterus receives its blood supply from the uterine artery, the ovarian artery and a branch of the urogenital artery. Nerve supply to the uterus consists of sympathetic fibers from the lumbar and lower thoracic region forming the uterine and pelvic plexuses. Nerve filaments from these plexuses supply the uterus, cervix, and proximal portion of the tubes. Parasympathetic fibers originate from the first to third sacral nerves and reach the plexus by way of the pelvic nerves or nervi erigentes.

In the **cow** the uterus is cornuate in shape, with the two uterine horns leaving the internal os of the cervix at an acute angle and lying nearly parallel to each other. The "uterine body" or proximal portion of the fused uterine horns with a single lumen is about 2.5 to 4 cm. long. Depending on the age and breed of the cow the horns are 20 to 40 cm. long and from 1.25 to 5 cm. in diameter in the nonpregnant state. The horns are joined by the dorsal and ventral intercornual ligaments for about

one-half their length. The uterus is located either on the floor of the pelvis, on the pelvic brim, or most commonly in parous cows over the brim on the caudal floor of the abdominal cavity. The uterus is usually dorsal or lateral to the bladder and is attached dorso-laterally by the broad ligament and the mesometrium. During pregnancy the uterus enlarges greatly and becomes located further cranially and ventrally in the abdominal cavity.

In the **mare** the nonpregnant uterus is cruciform or T-shaped with the horns perpendicular to the body of the uterus. The body is about equal in size to each horn, 15 to 20 cm. long, 4 to 7.5 cm. wide and 2 to 5 cm. thick. The uterus is suspended in the pelvic and abdominal cavities dorsal to the bladder by the broad ligaments. In the mare these ligaments are attached dorsally to the sublumbar region. The uterine horns in the mare lie ventral to the intercornual ligament. Unless gravid, the uterus usually does not lie on the floor of the pelvic or abdominal cavities.

In the **ewe** the uterus is shaped like that of the cow and located similarly. Each horn is 10 to 12 cm. long.

In the **sow** the uterine body is about 5 cm. long with long tortuous horns that are freely movable because of the long broad ligaments. In pregnant animals the horns may be 1.2 to 1.8 m. long.¹⁵

In the nulliparous medium-sized **bitch** and **queen** the uterus has a short body, 1 to 3 cm. long with straight horns 12 to 15 cm. long and 0.5 to 1.0 cm. in diameter that diverge at an acute angle toward the poles of each kidney. Suspended from the sublumbar region by the broad ligaments, the uterus lies entirely within the abdominal cavity.

The **cervix** (cervix uteri) is a tubular sphincter muscle between the vagina and uterus. Its wall is harder, thicker, and more rigid than are the walls of either the uterus or the vagina. This is more noticeable in uniparous than in multiparous animals. The blood and nerve supply are the same as those of the uterus and vagina with the exception of the ovarian artery.

The cervix in the **cow** is about 5 to 10 cm. in length by 1.5 to 7 cm. in diameter, the larger of the measurements occurring in pluriparous animals. In some Brahman or Brahman-cross, pluriparous cows the cervical dimensions may greatly exceed these averages. The cervix is located caudal to the uterus either in the pelvic cavity, on the pelvic brim, or in the abdominal cavity. During pregnancy the cervix is drawn forward into the abdominal cavity. The cervix of the cow is composed of 3 to 5 muscular fibrous transverse annular folds that have an almost cartilaginous consistency. The external os of the cervix does not protrude into the vagina, although prolapsed cervical rings in pluriparous cows may present

such an appearance. The cervix of the cow is difficult if not impossible to dilate manually. It dilates slightly during estrus.

The cervix of the **mare** is 5 to 7.5 cm. long and 2.5 to 5 cm. in diameter. It is suspended in the pelvic cavity caudal to the uterus and is characterized by numerous small low longitudinal folds of mucous membrane. The caudal os of the cervix extends into the vagina 2.5 to 5 cm. carrying with it a frenulum of vaginal mucous membrane below the external os. The cervix of the mare is relaxed, soft and easily dilated during estrus and tightly constricted and firm during diestrus.

The cervix of the **ewe** is about 2.5 to 5 cm. long and is similar to that of the cow. Its external os is located in the cranial ventral portion of the vagina and is partially covered by a projecting "hood" of mucosa.³

The cervix of the **sow, bitch and queen** is poorly defined, being characterized by a thickened wall with transverse folds. The sow's cervix is about 10 to 20 cm. long and is directly continuous with the vagina (See Figure 10). The cervix or neck of the uterus in the bitch is very short, 0.5 to 1 cm. in length and caudally the cervix projects into the vagina.

The **vagina** is a muscular membranous structure lying mostly retroperitoneally in the pelvic cavity dorsal to the bladder. It acts as a copulatory organ and as a passage for the fetus at the time of parturition. The vagina is capable of great dilation. Its caudal extremity is just cranial to the urethral opening in the region of the hymen or vaginovesibular junction. This junction is characterized in the mare, cow and sow by a slight constriction and annular folds.¹² A degree of persistence of the hymen, where in the embryo the paramesonephric ducts join the urogenital sinus, may occasionally occur. This may vary from a thin vertical central band to a completely imperforate structure. About 10 to 15 percent of heifers have hymenal remnants. These usually disappear after copulation or parturition. Prominent hymenal folds are present in the mare. A true hymen is lacking in the bitch and queen. The blood and nerve supply of the vagina arises from branches of the urogenital artery and autonomic nerves from the pelvic plexus. It is surrounded by loose connective tissue and varying amounts of fat.

The vagina of the **cow** is about 25 to 30 cm. long in the nonpregnant animal. The recto-genital pouch of peritoneum extends caudally about 12 cm. on the dorsal cranial surface and 5 cm. on the ventral cranial surface of the vagina. On the ventral floor of the vagina beneath the mucosa and running the length of the vagina, the two Gartner's ducts 0.25 cm. in diameter, remnants of the primitive mesonephric (Wolffian) ducts, are frequently

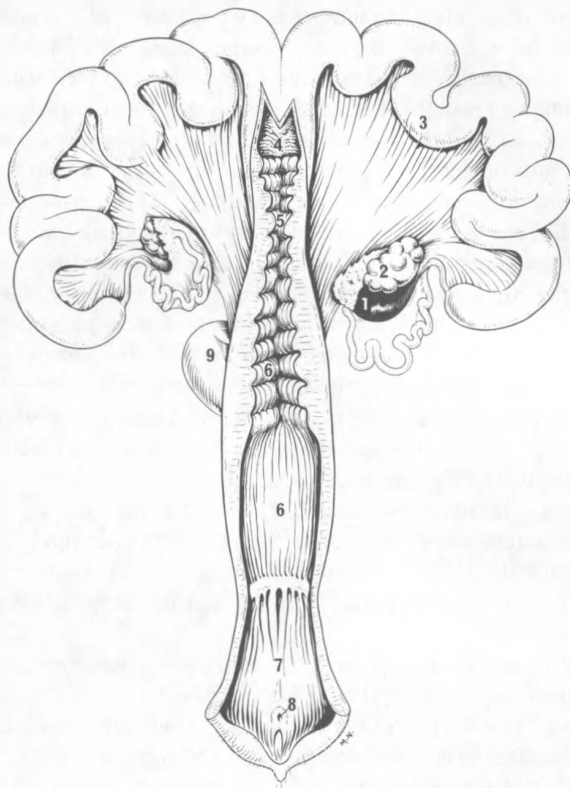


Figure 10. Genital organs of the sow. 1. Ovarian Bursa, 2. Ovary, 3. Uterine horn, 4. Uterine body, 5. Cervix, 6. Vagina, 7. Vestibule, 8. Clitoris.

present. Cysts of these structures may occasionally be observed.

The vagina of the **mare** is about 18 to 28 cm. long and 10 to 13 cm. in diameter when dilated. Most of the vagina, except a small dorsal cranial portion, is retroperitoneal. Mesonephric duct remnants are only occasionally present.

The vagina of the **ewe** is 7.5 to 10 cm. long and similar to the cow's vagina.

The vagina of the **sow** is 7.5 to 11.5 cm. long. It is small in diameter with a thick muscular coat. Mesonephric ducts are occasionally present.

The vagina in the **bitch** is long, 10 to 14 cm. and narrow, 1.5 cm. The muscular coat is thick, and mesonephric ducts are usually absent. A large dorsal median postcervical fold blends caudally into lesser dorsal longitudinal folds. The configuration of this fold and the lateral and ventral vaginal walls, when viewed through a speculum, simulates the external uterine ostium. This configuration of the vagina and vaginal portion of the cervix prevents or makes difficult, intrauterine cannulation.¹³ However, if the cervix is relaxed introduction

of fluid into the cranial portion of the vagina propels the fluid through the cervix and into the uterus. In the queen the vestibule and vagina are the same length.

The **vestibule**, located between the vulva and the vagina, and the **vulva** comprised of the two labia, the dorsal and ventral commissures and the clitoris, form the caudal termination of the genital tract. These two structures do not arise from the primitive paramesonephric ducts but rather from the ventral portion of the primitive cloaca. The ventral commissure of the vulva is pendulous and always lies ventral and caudal to the ischiatic arch.¹² The urethra opens into the cranial ventral portion of the vestibule. The vestibule has several circular or sphincter-like muscles that close the genital canal to the outside. These muscles are attached to the perineal body and the sphincter muscle of the anus and the caudal and last sacral vertebrae. Thus during parturition the vestibule acts as the point of attachment for the entire genital tract to contract upon when expelling the fetus. The clitoris is about 3 to 6 cm. long in the larger animals, but practically all of it is hidden in tissues between the vulva and the ischiatic arch. In the mare, bitch and sow the glans of the clitoris is well-developed and lies in a true fossa. The vulvar lips normally come together evenly, do not gape, and vulvar opening normally lies at a 90° angle to the pelvic floor. The vestibule and vulva are supplied with blood from the urogenital and the external and internal pudendal arteries and have the same autonomic innervation as the vagina. They are well-supplied by the sensory nerve fibers of the pudendal and caudal rectal nerves. The vulva and vestibule are the only reproductive organs of the female well-innervated by sensory nerve fibers.

The vestibule of the cow is about 10 to 12.5 cm. long on the ventral floor and 7.5 to 10 cm. long on the dorsal wall. Beneath the urethral orifice is the suburethral diverticulum, which is about 2.5 to 4 cm. long. The external visible portion of the clitoris in the cow is small in size. The major vestibular or Bartholin's glands, are two in number, one on each side, located in the constrictor muscles of the vestibule. They are about 1.5 to 3 cm. in diameter. These glands in the cow each open by a single duct in the lateral wall of the vestibule about 2.5 cm. caudal to the vagina.¹⁴

The vestibule of the **mare** is similar in size to that of the cow. Eight or 10 ducts from the minor vestibular glands open through its dorso-lateral wall. The external visible portion of the glans of the clitoris of the mare is large and prominent, 2.5 to 5 cm. long and 2 to 2.5 cm. wide. It is composed of erectile tissue similar to the penis. The clitoral fossa and sinuses of the mare are homologues of the preputial folds, and fossa glandis of the

stallion. The clitoral sinuses are 3 in number with the central sinus being the largest, located on the dorsal aspect of the glans clitoridis. The narrow openings of these sinuses are hard to detect unless the clitoris is partially extruded and held downward thus drawing them clear of the thin fold which separates the clitoral fossa from the vestibule.¹⁶ Contractions of the vestibular and vulvar sphincter muscles elevates the clitoris and protrudes it between the vulvar lips. This is called "winking."

The vestibule and vulva in the **ewe** are similar to that of the cow, but the suburethral diverticulum is very small. Minor, but not major, vestibular glands are present. The vestibule is about 2.5 to 3 cm. long. The clitoris is short, with the glans concealed in a fossa.

The vestibule in the **sow** is fairly long, about 7 to 9 cm. The labia are thick. The minor vestibular glands are variable in number. The clitoris is located about 2 cm. cranial to the ventral commissure. On either side of the cranial portion of the floor of the vestibule there is a cul-de-sac.

The vulva in the **bitch** and **queen** has thick labia. The vestibule is 2.5 to 5 cm. long. The urethral orifice opens on the urethral tubercle, which is elevated above the floor of the vestibule. There are small depressions on either side of the urethral orifice. Minor vestibular glands are present in the bitch but not in the queen which has two major vestibular glands. The clitoris in the bitch has a small, 0.6 cm. long by 0.2 cm. diameter, pointed glans and lies in a fossa. The dorsal commissure of the vulva is 8 to 9 cm. below the anus.

The anatomy of the perineal region of the cow and mare has been well-described.⁹

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EMBRYOLOGY OF THE FEMALE REPRODUCTIVE TRACT

The urogenital system is formed mainly from mesodermal tissue that in the early embryonic period forms the nephric and genital regions. The ovaries develop from the undifferentiated gonads that form late in the embryonic period in the genital or gonadal ridge located between the dorsal mesentery and the mesonephros. The

primordial germ cells from the wall of the yolk sac in the region of the hind gut have migrated into the gonads by the early fetal period. The surface epithelium of the female gonad gives rise to cortical cords that contain primitive germ cells, later called oogonia. The surrounding epithelial cells from the surface epithelium form the follicular cells. Thus secondary cortical cords are characteristic of the early female gonad. The ovaries remain in the abdominal cavity suspended by the mesovarial portion of the broad ligaments.

In both the male and female during the embryonic period, two pairs of genital ducts are formed that enter the cloaca, the mesonephric (Wolffian) tubules and ducts and the paramesonephric (Mullerian) ducts. The mesonephric duct development is described in the section on embryology of the male reproductive tract. The paramesonephric ducts arise as longitudinal invaginations of the coelomic epithelium in the same region as the mesonephric tubules and ducts. The cranial portion of the paramesonephric ducts differentiate in the female to form the uterine tubes while the caudal portions of the ducts unite or fuse to form the uterus, cervix and the cranial two-thirds or more of the vagina. The septum initially present between the two ducts in the caudal region disappears early in the fetal period. The caudal one-third or less of the vagina is formed by evaginations from the wall of the urogenital sinus. The hymenal region and annular folds are formed by the junction of the fused paramesonephric ducts and the urogenital sinus. In the male the paramesonephric ducts degenerate but portions may persist as remnants, the appendix testis, near the head of the epididymis, and the uterus masculinus be-

Table 2. Undifferentiated Genital Structures in the Embryo and Their Adult Male and Female Counterparts

Embryological Structure	Adult Female	Adult Male
Gonad	Ovary	Testis
Mesentery	Mesovarium	Mesorchium
Gubernaculum	Round ligament of the uterus and proper ligament of the ovary	Proper ligament of the testis
Paramesonephric duct (Mullerian duct)	Uterine tubes Uterus Cervix Vagina (cranial portion)	Appendix testis Uterus masculinus
Mesonephric tubules and duct (Wolffian duct and body)	Epoophoron Paroophoron (Parovarian or mesonephric duct or cysts) (Gartner's) ducts	Efferent ducts Epididymis Ductus (vas) deferens (ductuli aberrantes, appendix epididymis, paradidymis)
Genital tubercle	Clitoris	Penis
Genital folds	Vestibule	Penile urethra
Genital swellings	Vulva	Scrotum

tween the ampullae near the prostate gland. Portions of the mesonephric tubules and ducts may persist as remnants in the female forming the epoophoron on the cranial pole of the ovary, the paroophoron or parovarian cysts, and (Gartner's) ducts in the vaginal floor. (See Table 2).

Early in the fetal period the external undifferentiated genitalia become modified so the genital tubercle forms the clitoris, the genital folds, failing to unite as in the male, become the vestibule and the genital swellings enlarge to form the vulvar lips.

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Chapter II

EXAMINATIONS FOR PREGNANCY

An accurate, early diagnosis of pregnancy (cyesagnosis) in the cow, mare and sow has become essential for a successful, profitable breeding program. In recent years the owners of sheep and goats are recognizing the benefits of the early diagnosis of pregnancy. These benefits in the above herds of animals include a prompt assessment of the breeding efficiency of females, males or semen, and the management to maintain an acceptable parturition interval or to reduce the economically costly interval from parturition to conception. Pregnancy diagnosis increases the percentage of pregnant animals in a herd by the prompt treatment or culling of nonpregnant animals. An accurate pregnancy diagnosis is necessary in female animals bred, or possibly bred, either naturally or by artificial insemination prior to treatment for suspected failure of estrus. Most effective treatments would usually cause the expulsion of the conceptus in pregnant animals.

Pregnancy Diagnosis in the Cow

External or presumptive indications for pregnancy include:

(1) **Service by a bull or artificial insemination**—This information may not be known either through error, lack of records, lack of observation or accidental breeding.

(2) **Cessation of the estrous cycle and periods**—This is a moderately accurate means of diagnosis of pregnancy if the herdsman observes animals closely. It is not infallible since the herdsman may not see the signs of estrus or the animal may not exhibit signs of estrus ("silent" heats). About 15 to 30 percent of cattle not observed in estrus after service were not pregnant when examined rectally several months later.^{5,35}

After conception early embryonic death occurred in an estimated 10 to 25 percent of cattle based on the analysis of milk progesterone studies.^{7,33,34} Also uterine pathology such as pyometra and ovarian pathology such as cysts may occasionally cause cessation of estrous cycles in serviced but nonpregnant cows.

Conversely 3 to 6 percent of pregnant cows, especially

the first trimester of gestation, may occasionally exhibit signs of estrus.^{8,9,11,31} As in mares this estrus during pregnancy was apparently associated with follicular growth.

(3) **Radioimmunoassays (RIA) and enzyme immunoassays for determining progesterone levels** in blood plasma and milk have been developed in recent years and have proven helpful in monitoring the reproductive status, including pregnancy of cows. When the time of the prior estrus and breeding is known samples may be taken 21 to 23 days later. Milk samples are easier to obtain than blood samples and potassium dichromate can be added to milk samples as a preservative before shipping or long term storage.^{3b,14,15,29,26a,32}

Based on rectal palpation at 40 to 60 days after service, these tests for progesterone levels have proven to be 65 to 85 percent accurate for predicting pregnancy at 3 weeks post-service.^{6,15,17b,18,24,42} At this time a pregnant cow has a functional corpus luteum and a high level of milk and blood progesterone. When progesterone concentrations are low indicative of estrus and the absence of a functional corpus luteum and pregnancy, these tests have proven to be 94 to 100 percent accurate.

An enzyme immunoassay that may be an alternative to the radioimmunoassay for milk progesterone analysis for pregnancy diagnosis in cows has recently been described.^{26a} This test is simple, reliable and practical and with further refinement could replace the radioimmunoassay.

Each laboratory performing progesterone assays follows different procedures and thus different diagnostic levels of progesterone are reported. Progesterone is closely associated with the butter fat in milk so milk with high butter fat content will have a higher progesterone level than low fat milk. Thus procedures for sampling and interpretations of test results recommended by each laboratory should be followed.^{14,28,29,32,42}

The inaccuracies or high percentage (15 to 20) of false positive results of this test limits its value as a diagnostic test for pregnancy. Further confirmation of pregnancy by manual examination per rectum at a later date is indicated. Causes for this high incidence of error include: prior service of the cow at a time other than estrus; per-

sistence of the corpus luteum due to pyometra, presence of a luteal cyst, a sampling error, or possibly most frequently, early embryonic death from 15 to 50 days post-service. This test cannot detect failure of fertilization or early embryonic death prior to 10 to 14 days of pregnancy. When milk progesterone from cows of unknown pregnancy status was determined at three 7-day intervals, 97 percent of 88 pregnant cows and 98 percent of 83 non-pregnant cows were diagnosed correctly.²⁸

Manual rectal palpation of the genital tract of a cow by a skilled veterinarian at 20 to 23 days after service to detect the presence or absence of a functional corpus luteum or follicle, the turgidity of the uterine horns and the presence or absence of a clear or bloody vaginal mucus is equal to or more accurate than the progesterone assay in the detection of either pregnancy or the absence of pregnancy.

(4) **The presence or absence of postestrous bleeding**—"Menstruation" from the cow's vulva 24 to 48 hours after service is believed by some herdsmen to indicate conception. Careful studies have indicated that about 50 to 60 percent of cows and 75 to 85 percent of heifers exhibited some bleeding after estrus. There is no relationship between postestrous bleeding and conception.³⁹

(5) **Changes in the udder size of heifers and the size of the abdomen** in advanced stages of pregnancy—

In heifers increased development of the udder is noticeable about 4 months of gestation. In pluriparous cows enlargement and edema of the udder only occurs the last few weeks or month of gestation. Increased size of the abdomen is quite variable depending on the parity of the gestation. Young cows exhibit increased abdominal size after the sixth month of gestation and older cows after the seventh month of gestation. Progressive relaxation of the pelvic ligaments becomes evident the last month of gestation as does relaxation and edema of the vulva. Similar, but lesser, signs of relaxation of pelvic ligaments and edema and relaxation of the vulva may occur in cows with cystic ovaries.

(6) **Ballottement of the fetus or observation of fetal movements** after the sixth month of pregnancy. Occasionally in some thin animals where the fetus lies close to the abdominal wall, ballottement may be done as early as the fifth month of gestation. In fat animals this may not be possible until the eighth month of pregnancy. Depending upon the size of the fetus, the condition of the cow and the size and degree of fullness of the abdomen, the fetus can be ballotted in 5 percent or less of pregnant dairy cows at 5 months of gestation, 10 to 50 percent at 6 months, 70 to 80 percent at 7 months, 80 to 90 percent at 8 months and over 90 percent at 9 months. Abdominal ballottement of the fetus is easy in the cow

because of the relaxed, flaccid abdominal walls. The fist is pushed in an intermittent manner in a dorsal medial direction deeply into the lower right abdominal wall. If the fetus is ballotted, it is felt as a large, hard, solid object suspended or floating in the softer structures of the abdomen, such as the uterus, uterine contents and the abdominal viscera. The more advanced the pregnancy or the larger the fetus, the more dorsally in the right flank region the fetus may be ballotted.

(7) **Auscultation of the fetal heart** may be performed from the sixth to seventh month of pregnancy to term only with great difficulty due to the thick abdominal walls and viscera and the difficulty of obtaining a sufficiently quiet location. **Fetal electrocardiography** has been used to study the fetal heart and as an aid in the diagnosis of twin pregnancy and fetal mummification after the fifth month of pregnancy in cows.^{22,23,38}

(8) **Ultrasonography or the use of ultrasound to detect pregnancy** has only recently been developed to detect pregnancy in cattle^{1a,25a,b} (see Pregnancy Diagnosis in the Mare). Further research and improvement of the technique is necessary. Early pregnancy diagnosis with ultrasonography is more difficult in the cow because of the elongated rather than the oval blastodermic vesicle present in the mare, bitch and queen. Presently errors in diagnosis, especially in detecting nonpregnant cows, are too great for routine use of this technique when compared with the accuracy and lower costs of rectal palpation for pregnancy.

Internal indications of pregnancy in the cow

The rectal palpation of the uterus, ovaries, and uterine vessels is the most practical and accurate, as well as the earliest means of accurately diagnosing pregnancy in the cow. Prior to the actual rectal examination, the breeding history of the cow should be studied, including the date of the last calving, the dates and number of services, and information on any pathologic or disease condition previously affecting the reproductive organs. Complete breeding and reproductive records are very helpful for an accurate and rapid pregnancy or sterility examination of a cow or herd. Unfortunately many herds, especially range beef herds, do not have this information.²⁰

If a herd is to be examined it is helpful if someone is available to record notes on the results of the examination. The operator should wear proper protective clothing, consisting of rubber boots, a pair of clean, short-sleeved coveralls, or rubber pants, and a short-sleeved cloth jacket, and a thin rubber surgical, or disposable plastic glove and obstetrical sleeve. The sharp sealed edges of the plastic sleeve and glove often irritate and lacerate the rectal mucosa and anal skin. The glove and sleeve

is essential to protect the examiner's arm from chafing, infection, feces, and odor. It also protects the cow's rectum from irritation due to the examiner's hair and fingernails. No rings, especially rings with settings, should be worn on the examining hand. The fingernails should be short. Either hand may be used for the examination, but if many examinations are to be made it is usually desirable to use the stronger arm. Many prefer to do examinations with the left arm, so that the right is free for writing and for the manipulation of instruments or pipettes. The cow should be fastened or held securely to prevent forward or lateral motion. If many cows are to be examined it is helpful for an assistant to hold the tail away from the examiner's arm. Caution should be exercised when examining cows near posts or other obstructions that might cause the examiner injury if the cow moved suddenly. Cows seldom kick when being examined rectally but an excitable cow may occasionally kick backwards and injure the operator. When beef or range cows are in a chute a bar should be placed behind the cow above the hocks. Applying a nose lead or forcing the cow's tail dorsally and cranially in a firm manner may be necessary to restrain certain cows.

The arm should be well-lubricated with a non-irritating agent. The fingers and the hand are inserted into the rectum in the form of a cone. They are advanced into the rectum beyond the organ or structure to be palpated. Do not introduce the hand and arm a short distance into the rectum and push the rectum forward, thus stretching and irritating the rectal wall. With the arm well-inserted, bring a portion of the rectum caudally as a fold upon the hand and arm, thereby giving more freedom to the hand and producing greater relaxation of the rectum. It is usually necessary to remove most of the fecal material from the rectum before a thorough examination can be made. This can be done by raking the feces from the rectum with the hand, palm uppermost, or by stimulating peristaltic contractions and defecation by massaging the rectal wall just anterior to the anus and by allowing some air to enter the rectum. In the older, larger dairy cows one can leave the arm and hand in the rectum when a peristaltic wave is passed backward. However, in heifers and small beef cattle such a practice occasionally results in a laceration of the mucosa or even the rectal wall. In some cases, particularly where cattle have been on lush pasture and the feces are thin and loose, the rectal mucosa is easily irritated and the cow will suck air into the rectum, making examination nearly impossible through the dilated, tense rectal walls. Stimulating peristalsis, as mentioned above, will result in evacuation of the air. This may be aided and hastened by hooking the fingers cranially into a peristaltic contraction ring and pulling it

gently caudally. The cow's back should not be pinched down, since this tends to fill the rectum with air. Examinations of certain cows under epidural anesthesia may be desirable, however, ballooning of the rectum with air is a complication of this technique. All rectal examinations should be done with care, gentleness, and patience to avoid traumatizing the mucosa, rupturing the rectum, or irritating the anus.

The presence of free blood, or a fresh blood clot, in amounts of 15 to 30 ml. or more, not mixed with the feces, is highly indicative of a rectal rupture. If a rupture of the rectum occurs in the cow, examinations should cease immediately. Supportive treatment with penicillin and streptomycin, tetracyclines or sulfonamides and atropine are indicated. If the cow is not valuable, immediate slaughter may be indicated. If recovery follows rectal trauma with perforation, adhesions of the rectum to the genital tract, occasionally associated with abscesses, may occur.

A regular routine for examining the female genital tract should be developed and followed at each examination so no structure or portion of the tract will be overlooked. In making a rectal examination the hand is introduced cranial to the pelvic inlet or bony pelvis and is passed or swept from one side downward, across, and up the other side. If no structure is palpated the uterus is in the pelvic cavity. Usually the cervix or uterus is palpated on the brim of the pelvis in older cows. The hard, firm cervix is relatively easily located on the floor of the pelvis or cranial to it. The uterine cornua can be palpated in nonpregnant cows or in early pregnancy. The ovaries may be palpated lateral and slightly cranial to the cervix. As pregnancy develops they are drawn forward, especially the ovary corresponding to the horn containing the fetus, until by the fourth to sixth month of pregnancy they are out of reach. The uterus may be located laterally in the pelvic cavity if held there by a full bladder or a short broad ligament. The normal non-pregnant uterus in the heifer and pluriparous cow vary greatly in size. The uterus is normally soft, pliable and relaxed with a slight amount of tonicity in early pregnancy. A completely flaccid atonic uterus is characteristic of true anestrus and chronic cystic ovarian disease. At the time of estrus or following vigorous massage the uterus may become quite erect and turgid. In late estrus and early diestrus, 1 to 2 days after ovulation, the uterus may be thick-walled and edematous. Often about 20, 40 or 60 days post-conception the uterus may be quite tonic with a normal corpus luteum and an occasional follicle in the ovary.

The technique for manual retraction of the nonpregnant or one- to three-month pregnant bovine uterus into the pelvic cavity from the abdominal cavity to facilitate

its examination may be helpful.^{5,3} This involves caudal traction on the cervix, then further caudal traction on the ventral intercornual ligament. The cranial border of the broad ligament medial to the ovary may also be retracted. In particularly difficult cases the application of Knowles cervical forceps to the external cervical os will aid retraction of the uterus. The ovary may be grasped and slid between the middle and third fingers and held there while it is carefully palpated by the thumb and index finger.

Taking into consideration a number of factors including the age of the cow, rectal examination to diagnose pregnancy can be made quite accurately from about 35 days after conception. It is easier to detect early pregnancy in heifers than in cows. After 45 to 55 days of gestation, pregnancy diagnosis is usually easy for the experienced veterinarian. An accurate early pregnancy diagnosis is an important, economic necessity for the progressive cattle owner.

Veterinarians should be cognizant of the fact that the incidence of death of the early zygote, embryo and fetus in cows is highest during the earlier stages of gestation and declines rapidly after 60 to 90 days of gestation.^{5,21,33}

Early embryonic deaths occur whether rectal palpation of the uterus and its contents of fluids, membranes or amniotic vesicle, for confirmation of early pregnancy is performed or not. Recent studies on early pregnancy diagnosis using assays of progesterone in milk 21 to 23 days after service and continuing for 75 days have dem-

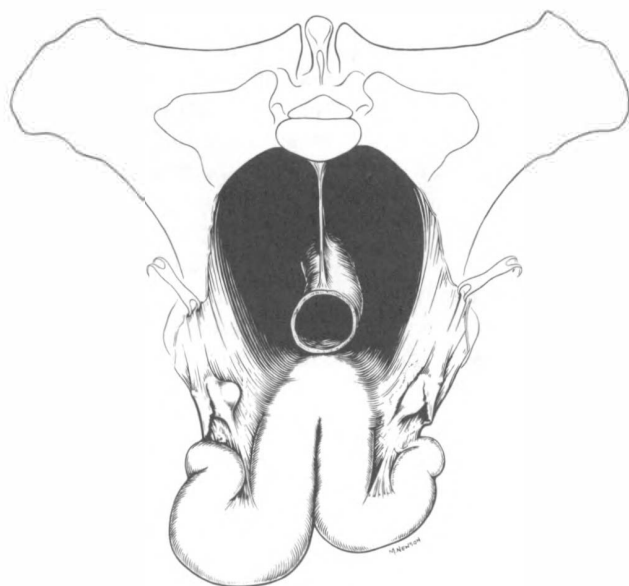


Figure 11. Uterus of a cow. 60 to 70 days pregnant.



Figure 12. Twin, bicornual bovine pregnancy, 60 days pregnant. Note CL in each ovary and lymphocytomas in the vagina. (Courtesy K. McEntee)

onstrated an incidence of early embryonic deaths of 7.2 to 14.5 percent in cows not subject to early rectal palpations of the uterus. These embryonic deaths were confirmed by a late return to estrus 28 to 60 days after service and rectal examinations at 55 to 75 days.^{7,21,33,34}

Vigorous, intense and prolonged rectal examinations for early pregnancy diagnosis, especially between 30 and 50 days of gestation, by certain, inexperienced examiners can result in an increased incidence of embryonic death and a return to estrus usually within 30 days but occasionally not until 50 to 90 days later.^{1,3,4,27,40} Palpation of the amniotic vesicle and slipping of the membranes were potentially more damaging to the developing embryo than palpation for the enlargement of the gravid uterine horn by fetal fluids or "fluctuance." The incidence of embryonic deaths were 4 to 9 percent in cows examined per rectum at 30 to 45 days of gestation compared to 2.5 to 4 percent when examinations were performed after 40 to 45 days of gestation.^{1,3,27,33,34} Since the "natural" embryonic death rate may be augmented by early pregnancy diagnosis per rectum, it behooves veterinarians to be particularly gentle and careful if early diagnostic examinations are made and possibly to reexamine and reconfirm the pregnancy diagnosis after 55 to 60 days of gestation.

As mentioned earlier under the use of progesterone



Figure 13. Uterus of cow 60 to 70 days pregnant. Note CL in the left ovary and large follicle in the right ovary.

assays for diagnosing pregnancy, rectal examinations of the cow's genital tract by a skilled veterinarian 19 to 23 days after service would be equally as accurate, about 75 to 90 percent, in assessing pregnancy at such an early date. If the cow failed to conceive estrus signs should be detectable including an erect, tonic uterus, an involuted, firm, small corpus luteum, a developing follicle, about 1 cm. in diameter, or a depression on the ovary where ovulation occurred. A vaginal examination by speculum should reveal the presence of an excess of clear, stringy mucus, possibly tinged with blood if ovulation has occurred, associated with a moderately hyperemic vaginal mucosa and a slightly relaxed external cervical os. If the cow conceived 19 to 23 days before the rectal examination one should detect a mature functional cor-



Figure 14. Sixty-day-old bovine fetus in the amniotic sac within the chorioallantoic membranes. Note beginning development of the cotyledons. (Courtesy K. McEntee)

pus luteum, the absence of a maturing or ovulated follicle, and a uterus that is somewhat flaccid and lacking the tone of a uterus under the influence of estrogens. A vaginal examination will reveal a pale mucous membrane, a closed cervical os and only a small amount of tenacious, thick mucus.

The definite or certain signs of pregnancy in the cow as determined by a rectal examination are: (1) The palpation of the enlarged horn containing the fluctuating placental fluids from 30 to 90 days of gestation. (2) The careful, very gentle palpation of the amniotic vesicle in early pregnancy from 30 to 50 days. (3) The slipping of the fetal membranes including the allantois chorion and its blood vessels upon gentle pinching of the uterus with the thumb and forefinger in early pregnancy from 40 to 90 days. (4) The palpation or ballotement of the fetus in the enlarged uterus containing fetal membranes and placental fluids after about 80 days. (5) The palpation of the placentomes after 100 days and (6) The palpation of the enlarged, thin-walled, "whirring" uterine arteries after 90 days of gestation. Less definite signs of pregnancy include the increase in size of the uterus and a thinning and distension of its walls, its location in the abdominal cavity, the location, size and persistence of the corpus luteum and vaginal changes.

Uterine changes during pregnancy: During early pregnancy, the uterine horns, especially the horn containing the embryo or fetus, increase in size due to the distention of the horn by the amniotic vesicle, placental fluids, the membranes, and the conceptus. This increase in the diameter of the uterine horns is characterized by a thinning of the uterine wall and a fluid, watery, "alive" fluctuating feeling on palpation of the uterine horn. The uterine horns have a fair amount of tone due to their tenseness and distention. From 40 to 90 days of pregnancy, the uterus feels somewhat like a thick rubber balloon nearly filled with water. The approximate size of the horn containing the fetus during the first 5 months of pregnancy is given in Table 3.

Since the size of the fetus is small during the early stages of pregnancy the amount of fluid in the uterine horn largely determines its size or diameter. The volume of fluid increases rapidly the first 5 months of pregnancy but increases more slowly after the fifth or sixth month (Table 3). In cattle there is a marked increase in the allantoic fluid volume between 40 and 75 days and 6-1/2 and 7-1/2 months of gestation and a marked rise in amniotic fluid volume between 3-1/2 and 4 months of gestation that is not reflected in the total volumes of placental fluids given in Table 3.²

The size of the amniotic vesicle varies as noted in Table 3. The amniotic vesicle is spherical in outline up

Table 3. Size and Characteristics of the Bovine Fetus and Uterus during Pregnancy*

Days of Gestation	Diameter of the Horn Containing the Fetus	Amount of Fetal Fluid	Diameter of the Amniotic Vesicle	Length of the Fetus (C-R)	Weight of the Fetus	Diameter of the Placentomes	Diameter of the Uterine Artery	Fetal and Placental Characteristics
30	2-4 cm	30-60 ml	1.0 cm (pea size)	.8-1 cm	.3-.5 gm			Head and limb buds recognizable, placenta not attached.
40	3-6 cm	75-100 ml	2.5-3.0 cm (size of plum)	1.75-2.5 cm	1-1.5 gm			
50	5-7 cm	90-200 ml	3.5-5.0 cm (1-1/2-2")	3.5-5.5 cm	3-6 gm			
60	6-9 cm	200-450 ml	6-7.5 cm	6-8 cm (mouse size)	8-30 gm			Claw buds and small scrotum recognizable, palate and sternum closed, placenta attached and lens-sized cotyledons present.
70	7-10 cm	350-650 ml		7-10 cm	25-100 gm	0.5-0.75 cm		
80	9-12 cm	500-800 ml		8-13 cm	120-200 gm	0.5-1.0 cm		
90	10-13 cm	750-1400 ml		13-17 cm (rat size)	*200-400 gm	1-1.5 cm (size of dime)	0.3-0.5 cm	Hair on lips, chin and eyelids, scrotum present.
120	12.5-18 cm	2000-3500 ml		22-32 cm (small cat size)	1000-2000 gm	1.5-2.5 cm (size of quarter)	0.5-0.8 cm	Fine hair on eyebrows, claws developed and yellow-colored, epithelial plaques present on amnion, horn pits present.
150	18-23 cm	4000-5000 ml		30-45 cm (large cat size)	3000-4000 gm	2.5-4 cm (size of 1/2 dollar)	0.6-1.0 cm	Hair on eyebrows and lips, testes in the scrotum, teats developing.
180		4000-7500 ml		40-60 cm	5-10 Kg.	4-5 cm	0.9-1.25 cm	Hair on inside of ear and around the horn pits, tip of tail and muzzle.
210		6300-10,000 ml		55-75 cm	8-18 Kg.	5-7.5 cm	1.25-1.5 cm	Hair on metatarsal, metacarpal and phalangeal region of extremities and beginning on the back, long hair on tip of tail.
240		8000-12,000 ml		60-85 cm	15-25 Kg.	6-9 cm	1.25-1.7 cm	Fine short hair all over the body. Incisor teeth not erupted.
270		12,000-20,000 ml		70-100 cm	20-50 Kg.	8-12 cm	1.5-1.9 cm	Hair coat complete and long, fetus large, incisor teeth erupted.

*Richter & Goetze, Fraser, Bongso and Basrur, Swett, Matthews and Fohrman, Gier and Marion, Zemjanis, Arthur, Winters, Green, Comstock, Ball, Evans and Sack and Eley et al. These are all approximate figures as there is much individual variation especially between heifers and cows.

to about 40 days, at which time it becomes oval. The palpation of the amniotic vesicle in the free most distended portion of the horn at 30 to 65 days of pregnancy is helpful in diagnosis because of its fairly tense spherical to ovoid shape. If the vesicle is not palpable or is small or collapsed the embryo may have died and is macerating. If the operator is experienced, skillful and gentle early embryonic death may be detected at 30 to 40 days of gestation by palpation of the amniotic vesicle.^{3,36} These embryos are probably resorbed. Palpation of the amniotic vesicle should be performed very carefully and gently to avoid damaging or rupturing it or the heart or other friable organs of the embryo. The fingers and thumb gently palpate the gravid horn and as they are moved slowly back and forth the vesicle can be felt to slip between them. If such an examination cannot be done skillfully and gently it is best to omit it as it is not necessary for an accurate pregnancy diagnosis.

Slipping of the fetal membranes is another aid to early pregnancy diagnosis in the cow that is best performed from 35 to 90 days of gestation. Prior to 40 days of gestation slipping of the fetal membranes is difficult to detect because the membranes are thin and fragile. The technique consists of gently picking up and pinching or compressing either horn of the uterus and feeling the fetal membranes, the allantois chorion and its vessels slip between the thumb and the fingers before the uterine wall escapes from between the fingers.^{3,5,13} The entire horn may be grasped and let slip through the fingers so that the connective tissue band and allantoic vessels on the lesser curvature of the uterus, which are three to four times thicker than the chorioallantoic membrane, can be palpated. Excessive or rough pinching of the uterus, particularly over the amniotic vesicle is to be avoided, to prevent damage to the embryo or fetus. This technique of slipping the membranes is especially valuable in the differential diagnosis of pregnancy from uterine diseases characterized by fluids causing uterine distention, such as pyometra or mucometra.

Location of the pregnant uterus in older cows, since the uterus in the nonpregnant state lies on or over the brim of the pelvis, the pregnant uterus is found in the abdominal cavity as early as at the time of conception to the second to third month of pregnancy. In all ages of cattle the uterus lies on the floor of the abdominal cavity after the fourth month of pregnancy. In uteri that hang forward in the abdominal cavity the allantoic fluid tends to gravitate to the apices or pendant portions of the uterus frequently out of reach of the operator unless he retracts the uterus into or towards the pelvic cavity. In heifers or young cows 2 to 3 months pregnant, the uterus often lies in the pelvic cavity and the horn containing the fetus exhibits a typical dorsal bulging or terracing

because of its location. By the fifth to sixth month of pregnancy in all cows the uterus is drawn well-forward and downward in the abdominal cavity so that in some cases only the cervix and uterine vessels can be palpated per rectum. By the sixth to seventh month the fetus becomes large enough so that it can again be palpated on rectal examination in nearly all cows; and by the eighth or ninth month the fetus may, in a few cows, actually extend caudally so that the nose and feet are resting in the pelvic cavity. As the uterus drops forward into the abdominal cavity during pregnancy the mesometrium stretches and thickens and the ovaries are also drawn ventrally and cranially. The ovaries can usually be palpated through the fourth month of gestation and occasionally during the fifth month. During the latter month the ovary on the side of the uterine horn containing the fetus is usually drawn out of reach of the hand in the rectum.

Fetal size and characteristics at various stages of pregnancy:

The statistics of bovine fetal, length, and weight have been recorded by a number of authors. The average figures and records given by these workers are noted in Table 3. The author estimates that the fetus may be palpated per rectum in over 95 percent of cows at 3 to 4 months of gestation, about 40 to 70 percent of cows at 5 and 6 months of gestation, about 80 percent of cows at 7 months and about 95 percent or more of the cows at 8 to 9 months of gestation. Palpation of the fetus before 60 to 70 days of gestation is not possible because of the tense, distended amniotic vesicle and the small size of the embryo or the fetus. Between 70 to 120 days fetal crown-to-nose or head size measurements are 1.5 cm. at 70 days, 5.5 cm. at 90 days and 9.0 cm. at 220 days.³

The larger and deeper the abdomen of the cow and the longer the mesometrium the greater the difficulty in palpating the fetus per rectum during midgestation. Thus in heifers the fetus can often be palpated per rectum the entire gestation period. If the fetus cannot be felt, pregnancy diagnosis is based on the position of the uterus, the size of the uterine arteries, the palpation of the placentomes and the slipping of the fetal membranes. After the sixth month of pregnancy one can elicit or cause fetal movements by pinching the claws, grasping and pulling a fetal leg, pinching the eyeballs, or grasping the nose of the fetus either through the rectal or vaginal wall. The latter is possible only during the last month or so of pregnancy. If the bovine fetus can be secured and measured an approximation of its age, especially up to 6 months of age, as thereafter there is too much variation between breeds, may be obtained by doubling the crown-rump

length in inches and taking the square root of the result which is equal to the months of gestation.⁴

Palpation of placentomes Although the placentomes are forming by 60 to 70 days of pregnancy, they seldom can be palpated as definite structures until 75 to 80 days. At this time they can be palpated in the uterine wall at the level of the intercornual ligaments of the horn containing the fetus as ovoid thickened areas. They increase in size as the fetus develops (see Table 3). Inexperienced examiners may mistake a placentome for the ovary between 110 and 180 days of gestation. In general the placentomes in the middle of the horn containing the fetus and nearest the attachment of the middle uterine artery are larger than those placentomes in the cervical or apical end of the horn or in the opposite nongravid horn. Thus the largest placentomes from the fifth month of pregnancy to term are usually out of reach of the rectal hand.

The development and enlargement of the uterine artery is closely associated with the size of the fetus and the duration of pregnancy. The artery supplying the greatest amount of blood to the uterus is the uterine artery. Palpation of changes that occur in the size of this artery and the character of its pulse are of diagnostic value. The uterine artery arises from the internal iliac artery close to its origin at the aorta. In the nonpregnant cow it curves caudally in the broad ligament over the dorsal part of the shaft of the ilium into the pelvic cavity and then downward and forward over the pelvic brim to enter the concave aspect of the uterine horn near its center. As pregnancy progresses the artery is pulled more cranially as the uterus drops forward in the abdominal cavity until in the latter half of pregnancy it may be located 5 to 10 cm. cranial to the shaft of the ileum. One should not confuse the internal iliac artery which is securely fastened by fascia to the shaft of the ileum with the uterine artery in the broad ligament which is movable for a distance of 10 to 15 cm. In heifers a change in the size of this artery to the horn containing the fetus may be noted as early as 60 to 75 days of pregnancy, when it may be 0.15 to 0.3 cm. in diameter. In older cows the change in size of the middle uterine artery to the horn containing the fetus can be noted at 90 days, when the artery is about 0.3 to 0.45 cm. in diameter. The approximate size of the artery at different stages of gestation are noted in Table 3. The uterine artery to the nongravid horn also enlarges but the changes are not so great as those in the artery to the gravid horn and they occur later. With the enlargement of the artery the arterial wall becomes thinner, so that instead of feeling a pulsation in the artery a characteristic "whirr," "thrill" or fremitus is felt. This is first recognized at about 80 to 120 days of pregnancy, but the time may be variable.

By the fourth to fifth month of pregnancy it is always palpable. If the uterine artery is pressed too tightly this fremitus may stop, so that only a pulsation is felt. In advanced pregnancy this artery, when palpated lightly, feels much like a stream of water surging intermittently through a thin rubber hose. Aneurysms producing localized fremitus of the uterine artery in the cow may rarely be present. This change in the size of the artery and the character of the pulse is helpful in diagnosing pregnancy about the fifth and sixth months, when the uterus is forward in the abdominal cavity and the fetus cannot be palpated. It is of value and aid in determining the stage of pregnancy. If both uterine arteries are equally enlarged, twin bicornual pregnancy should be suspected. The characteristic fremitus of the pulse is often of value in determining whether or not a normal pregnancy with a viable fetus is present.

Determining the stage of gestation up to 120 days by rectal palpation when the date of service is unknown is quite precise, to within a few to 10 days but as gestation progresses it becomes less precise due to individual and breed variations in the size of the uterus and fetus.

The horn of the pregnant bovine uterus not containing the fetus may vary greatly in size. In most bovine pregnancies a portion or usually all of the non-gravid horn takes part in the placental attachments. There is a progressive enlargement of the nongravid horn, its uterine artery, and placentomes but these changes are not as great as those of the gravid horn. In possibly 10 to 20 percent of cows, some or most of the caruncles and cotyledons in the nongravid horn fail to develop normally or may be absent, in which case this horn is smaller than normal or even is nonfunctional. As a result an excessive burden may be placed on the gravid horn, with an hypertrophy of the placentomes causing them to become 15 cm. in diameter in some cases.

Examination of the ovaries. The ovary may be gently grasped between the first and second or second and third fingers and palpated with the thumb. The ovary following ovulation develops a corpus luteum at the site of the ruptured follicle. If fertilization and development of the ovum and embryo proceed normally this corpus luteum persists throughout pregnancy in the cow. The corpus luteum of pregnancy, or corpus luteum verum, is slightly larger, 2.46 cm. in diameter and 6.5 gms. in weight, than the corpus luteum of the estrous cycle, 2.3 cm. and 5.7 gms., respectively. These small differences are of no diagnostic value.¹⁰ However, as pregnancy progresses the corpus luteum tends to develop a darker golden-brown color and its projection above the surface of the ovary is less prominent due to a heavy layer of epithelium and stroma that covers it. It remains essentially the same size until near parturition.

With few exceptions the corpus luteum of pregnancy is on the ovary corresponding with the horn of the uterus containing the fetus. Less than 1 percent of the corpora lutea of pregnancy were in the ovary opposite the horn containing the fetus.^{1,2,5a,12} Thus, more than 99 percent of cows have the corpus luteum of pregnancy on the ovary corresponding to the horn containing the fetus. The possible reasons for the presence of the corpus luteum being on the ovary opposite the horn containing the fetus might include: (1) External migration of the ovum across the peritoneal cavity. This is highly unlikely. (2) Internal or transuterine migration of the early embryo through the uterine body, which is rare in the cow.^{32b} (3) Regression of the corpus luteum of pregnancy and the development of another corpus luteum on the opposite ovary. This has been observed by the author during the first trimester of pregnancy in 3 cows.

If a rectal examination of a cow 20 to 24 days after service reveals a normal corpus luteum on one ovary and no signs of estrum, the examiner can be reasonably sure that conception has taken place. These early diagnoses are about 80 to 90 percent accurate. This can be confirmed on re-examination at 40 to 50 days by the presence of the corpus luteum in the same site on the same ovary with typical changes occurring in the gravid uterine horn. The manual removal of a bovine corpus luteum of pregnancy or the administration of a prostaglandin the first 5 months of gestation will invariably result in abortion.

Vaginal changes during pregnancy as determined by examination with a vaginal speculum and light or manually may be of some diagnostic value but are of only secondary importance to the uterine changes. During pregnancy the vagina usually develops a pale, dry, sticky mucous membrane similar to that observed in diestrus. The external os of the cervix is closed and pale. Since milk or serum progesterone levels and vaginal electrical resistance correlate closely, a commercially-produced instrument to measure the latter as an estrus-detection aid may be of value for early pregnancy diagnosis.^{24a} In about 60 to 70 percent of the cows the cervical seal which forms after conception increases in size until it protrudes or covers the external os and is visible and palpable between 40 to 120 days of pregnancy. In the rest of the cattle it is present in the cervical canal but does not become visible. The seal is a translucent, whitish mucus that is very tough, adhesive, and tenacious. This seal may remain after the fetus has died in such diseases as mummification of the fetus and trichomoniasis with fetal maceration. Occasionally there may be a normal pregnancy with a cervicitis of the external os and a purulent vaginitis. In such an instance, the cervical canal and internal os have a normal cervical seal present. There is

in rare cases a condition characterized by a cervical seal of large proportions called mucocervix. This is noted by a cervix with a diameter of 7.5 to 10 cm. filled with tenacious mucus and accompanied by a persistent corpus luteum or luteal cyst and a failure of estrum. Just prior to parturition and abortion the normal cervical seal breaks down and is discharged in strings. The vaginal mucous membrane becomes more moist and hyperemic, and the cervix relaxes and dilates. Thus a vaginal examination is of value in diagnosing impending abortion or parturition. Passing a catheter or insemination pipette through the sealed cervix in a pregnant cow may introduce infection into the uterus and cause the death of the fetus the release of prostaglandin and subsequent abortion. In advanced pregnancy a manual examination of the vagina frequently reveals the presence of a portion of the uterus and fetus in the pelvic cavity dorsal or lateral to the vagina. The cervix is pulled forward by the weight of the gravid uterus causing a lengthening of the vaginal cavity.

Biologic tests for the diagnosis of pregnancy in the cow have been reported but are not as accurate as the rectal diagnosis of pregnancy by a competent veterinarian. Presently the only practical biologic test for pregnancy in the cow is the radioimmunoassay (RIA) test for determining the levels of progesterone, produced by a functional corpus luteum, in the milk or blood plasma as described previously.

Differential Diagnosis in Pregnancy Examinations

Anatomically there is no reason for confusing a pregnant uterus with such structures as the **bladder**, the pendulous **left kidney** or the **rumen**. Careful rectal examination, consideration of the anatomical structure and relationships of these organs and their consistency, will prevent erroneous diagnoses.

Tumors may be confused with pregnancy in the cow if a careful examination is not performed. The tumors most commonly confused with pregnancy are lymphocytoma, granulosa cell tumor of the ovary, and fat necrosis in the mesentery. Other tumors of the uterus or genital tract of the cow such as leiomyomas and fibromas that might be confused with pregnancy are rare.

Mummification of the bovine fetus characterized by the death of the fetus from 3 to 8 months of gestation, failure of abortion, absence of estrum or parturition, absorption of the fetal and placental fluids, contraction and thickening of the uterine walls, resorption of the placentomes, and the presence of the hard, firm fetus and

membranes in the closely applied uterine horn lying deep in the abdominal cavity may be confused with pregnancy. The history of apparent conception but failure of udder development, failure of an increase in the size of the abdomen or fetus, and failure of parturition should cause the examiner to suspect the presence of this condition. On rectal examination the uterus is usually drawn forward into the abdominal cavity and may require caudal traction on the cervix or lifting of the ventral abdominal wall to bring it within reach of the rectal hand. The typical "whirring" or fremitus in an enlarged uterine artery is absent. If palpable, the ovary on the side of the horn containing the fetus has a corpus luteum of pregnancy. Mummification of the fetus has not been associated with rectal palpation of the uterus for pregnancy diagnosis even when the examinations have been vigorous and prolonged.

Pyometra or accumulation of pus, from 200 to 20,000 ml. in amount, in the uterus is characterized by failure of estrum and may be confused with pregnancy. Pyometra may occur either postpartum or post-service. In most cases pyometra follows a retained placenta and postpartum metritis, in which case there is frequently an intermittent discharge of pus from the vagina. In trichomoniasis or other infections early pregnancy may occur and the fetus may be killed by the organisms. The fetus and fetal membranes then macerate with pyometra resulting. In these cases the cervical seal may remain intact in the cervix for long periods. In pyometra the uterine walls are usually thick and heavy and lack tone. The fluid in the uterus may be watery, syrup-like or viscous. The uterine horns are usually unequal in size as in pregnancy. The pus tends to gravitate and collect in the pendant portion of the horns and there is no dorsal bulging of the horn as in often palpated during early pregnancy. The fetus or placentomes cannot be palpated and the fetal membranes cannot be slipped. The uterine arteries are usually contracted and the fremitus is absent. If the diagnosis is uncertain, reexamination in one to two months is indicated. In normal pregnancy progressive development of the fetus and uterus occurs, whereas in pyometra the condition remains essentially the same. As in mummification of the fetus the corpus luteum remains in the ovary.

Maceration of the fetus exhibits signs similar to those of pyometra with the exception that death of the fetus after the fourth month of pregnancy results in the presence of fetal bones in the uterus causing crepitation when palpated. Occasionally the cervical seal breaks down and a vaginal discharge is observed.

Mucometra or hydrometra may occur secondarily to an imperforate hymen, in the defective horn of a cow with uterus unicornis, in other anomalies of the devel-

opment of uterus, cervix, or vagina, segmental aplasia, and in long-standing cases of cystic ovaries causing a cystic degeneration of the uterine wall. This condition is variable in its manifestation. Anomalies of the development of the paramesonephric duct system may not be characterized by failure of estrum, whereas in cystic ovaries failure of estrum is common. The mucus varies in consistency from a thin, watery secretion seen in cystic degeneration of the uterine wall, to a heavy mucus secretion in heifers with imperforate hymens, to a gummy and inspissated type of mucus that might be confused with a mummified fetus in certain defects including segmental aplasia of the uterine horn. The uterine wall in most of these conditions is fairly thin but in cystic degeneration of the uterine wall it may be so extremely thin that it is difficult to palpate. These conditions differ from pregnancy based on the history; and on rectal examination by a failure to "slip" or feel fetal membranes, by the absence of the fetus and placentomes, lack of fremitus or increase in size of the uterine artery, and a failure of the progressive development of the uterus as in a normal pregnancy.

Embryonic or early fetal death with abortion or possible absorption. Death of the embryo or fetus prior to 70 to 90 days of gestation may be followed by immediate or occasionally delayed abortion.⁴ In early pregnancy the fetal membranes may continue to grow and develop for several weeks after fetal death before showing degenerative changes. Thus a positive diagnosis of fetal death and absorption can only be made late in the absorptive process when the signs of pregnancy do not correspond with the breeding history, a diminished amount of fetal fluids are in the uterus, the membranes feel collapsed and wrinkled upon slipping between the fingers and thumb, the amniotic vesicle may be atonic and flaccid or be absent, and the uterine wall is thick and somewhat contracted. These cases when detected or suspected should be brought to the attention of the owner so that he can watch the cow closely for a recurrence of the estrous cycle or if this is not observed the cow can be reexamined two to four weeks later. Probably in most of these cases, expulsion or abortion of the degenerated partially macerated embryo and its membranes occurs and is unobserved.

Careful rectal examination may reveal abnormalities or pathology of the pregnant uterus and fetus in such conditions as hydrops amnii and allantois, fetal monsters, twins, torsion of the uterus, adhesions of the pregnant uterus to other abdominal structures, rupture of the uterus with an extra-uterine fetus, metritis characterized by lack of tone of the uterus and gaseous crepitation within the uterus that occasionally precedes bacterial abortion.

The diagnosis of twins may be based on the findings

of equal enlargement of both uterine horns or uterine arteries, the presence of two amniotic vesicles, or the presence of two fetuses—usually one in each horn, but occasionally two in one horn. In most cases there are two corpora lutea, usually one on each ovary, as bicornual twins are by far more common than unicornual twins. Dizygotic bovine twins are much more common than monozygotic twins.

There is ample evidence to indicate that in the dairy cow the right ovary is slightly more active.^{1a,5a,12,13} About 60 percent of pregnancies occur in the right horn and 40 percent in the left horn. In beef cattle these percentages are more nearly equal.¹²

PREGNANCY DIAGNOSIS IN THE MARE

The external indications of pregnancy in the mare are similar to those in the cow. Since the breeding season for most mares is short, early and accurate pregnancy diagnosis is essential in a good breeding program. Following service the mare should be teased regularly by a stallion or an aggressive, or testosterone-primed gelding every one to two days to determine the end of estrus, and continuing for 18 to 21, and even to 40 days to determine if conception has apparently occurred. It is not unusual for up to 10 to 15 percent of pregnant mares to exhibit some or all the signs of estrus, especially the first several months of gestation.^{20,50} These signs are usually weak and short, lasting for only one or two days. They are probably due to developing ovarian follicles that regularly occur in mares the first 90 days of gestation. Other mares may show no signs of estrus after breeding and yet have failed to conceive. Post-estrous bleeding as seen in cattle after estrus does not occur in the mare.

Diagnosis of pregnancy in the mare based on an increase in the size of the abdomen is hazardous even though most mares in advanced pregnancy show a marked increase in the size and a characteristic shape of the abdomen. The pregnant mare's abdomen after the fifth to sixth month of pregnancy is usually pear-shaped with the greatest width in the ventral third. In fat mares or mares fed large amounts of roughage the abdomen is large but round with the greatest width in the middle third. The last month of pregnancy the mammary glands begin to enlarge. Distention of the teats with colostrum occurs the last 3 to 4 days of gestation and in most mares "waxing" of the teats due to the expression of colostrum occurs 4 to 48 hours before foaling. This may be absent or in a few mares may occur for three to ten days before foaling. Edema of the abdomen just anterior to the udder

may occur in advanced pregnancy. Relaxation of the pelvic ligaments occurs in late gestation but is not as evident in the mare as in the dairy cow.

Ballottement of the fetus in the mare in advanced pregnancy is difficult due to the thick abdominal wall and because the mare will tense the abdomen. Ballottement in the mare, however, is occasionally possible on either or both sides of the abdomen. Fetal movements may be observed through the abdominal wall the last months of pregnancy especially after the mare has ingested cold water. Prior to parturition the vulva becomes enlarged, flaccid, and edematous.

Plasma and milk progesterone values, determined by radioimmunoassay techniques, as in the cow, have been shown to be helpful in determining the reproductive status of mares, including the stages of the estrous cycle and the diagnosis of early pregnancy. However several days are usually required for transporting and laboratory procedures on the samples. Progesterone levels are probably more reliable than behavioral patterns toward a teaser stallion in assessing ovarian activity in certain mares. This test would be of value for bred mares when no stallion was available for teasing or for mares exhibiting poor estrous behavior. Plasma samples from all mares were more easily obtained and processed than milk samples from lactating mares and produced equally accurate results. In a limited study over 90 percent accuracy was obtained in the diagnosis of pregnancy by the presence of high levels of plasma progesterone 16 to 17 days after bred mares went out of estrus. These diagnoses were later confirmed by rectal palpation. Low levels of plasma progesterone indicated non-pregnancy and the presence of estrus at this time.^{24b,29} Persistence of the corpus luteum without pregnancy is not uncommon in the mare and could cause an occasional inaccurate early pregnancy diagnoses when large numbers of mares are examined.^{3b,24b,28,29}

Ultrasonography or ultrasonic echography of the genital organs of the mare shows definite promise of being very useful in the detection of early pregnancy.^{8b,34b,40,44a,b,49b,c,56a,57a} Although this technique involving the use of a rectal probe or transducer, requires further study and refinement and the equipment is very costly (\$13,000 to \$28,000) (see footnotes 1–5), research has shown that pregnancy diagnosis for the presence of a chorionic vesicle or conceptus may be per-

(1) ADR-Advanced Diagnostic Research, 734 W. Alameda Dr., Tempe, Ariz., 85282; (2) ATL-Advanced Technology Laboratories, 13208 Northrup Way, Bellevue, Wa., 98007; (3) Bion Corporation, 7000 N. Broadway, Bldg 1, Suite 105, Denver, Colo., 80221; (4) Fischer Ultrasound ('Vetscan') 10516 United Parkway, Schiller Park, Ill., 60176; (5) Westmed, 801 Dexter Ave, North Seattle, Wa., 98109.^{8b}

formed without damage to the embryo with an accuracy of over 95 percent from 15 to 50 days of gestation. Repeated examinations at 5 to 10 or more day intervals greatly reduces the possibility of error as the size of the normal viable vesicle grows at a steady rate from about 1.5 to 2 cm. in diameter at 15 days of gestation to 2.75 cm. at 20 days, to 3.25 cm. at 25 days, 3.6 cm. at 30 days, 4.45 cm. at 35 days, 6.0 cm. at 40 days and 8.85 cm. (range 7–10 cm.) at 50 days. The viable embryo increases in size from about 1 cm to 3.5 cm from gestation day 15 to 50.^{34b,49c,56a} In early pregnancy diagnosis errors may be due to scanning near the tip of the uterine horn and locating an ovarian follicle or in older mares finding an endometrial cyst or enlarged lymphatic lacunae in the uterus.^{34b,56a} In one study^{49c} 11 of 67 mares (16.4%) had a resorption or death of the embryo between 15 and 50 days of gestation. This ultrasound instrument has also proven valuable in the detection of twin embryos early in gestation when treatment is best accomplished.^{34b,56a} Presently many veterinarians are using this instrument on horse farms in England, France and the U.S. Further controlled studies are indicated to assess its value and possible harmful effects, which presently are negligible, and to obtain needed data on the incidence and fate of early twin embryos and early embryonic deaths in mares. Fetal pulses are visible at 24 days. Ultrasound is useful in the diagnosis of pregnancy and fetal monitoring in dogs, cats, sheep, cattle and goats as well as the mare.^{43b}

The accuracy of an ultrasonic pregnancy detector with the transducer applied to the external abdomen of the mare was unsatisfactory.^{49b,57a}

Fetal electrocardiography has been found to have some technical limitations for the diagnosis of early pregnancy and twinning. Further studies will be necessary if this technique is to become practical.^{12,27,33,34}

Internal examination for pregnancy in the mare.

Before the internal examination for pregnancy in the mare is performed, a good breeding history should be obtained if possible. The foaling and breeding dates, dates of estrum, the frequency and efficiency of teasing before and after breeding, and knowledge of the regularity of the mare in her estrual cycles and past foalings are helpful.

The rectal diagnosis of pregnancy in the mare by an experienced veterinarian is presently one of the earliest and most accurate methods available. In performing a rectal examination of a mare the same equipment, dress, and mode of procedure is used as for examinations of the cow, with the following exceptions. Restraint is more essential in mares. Since most horses are more accustomed to being handled on the left or near-side, the author prefers to perform rectal examinations with the right

arm and make the initial anal penetration while standing lateral to the left hip of the mare. Thus both the operator and the man on the twitch or halter are on the same side of the mare. Many mares require the application of a nose twitch to control and make them stand quietly and prevent them from kicking the operator. Some veterinarians have the mare's tail forced firmly dorsally and cranially over the sacrum as a further form of restraint. Certain excitable mares that object to restraint must be handled gently and quietly if a rectal is to be performed. Often these mares may be examined by having only a foreleg elevated. In some mares tranquilization or even sedation may be required as well as application of a twitch. If breeding hobbles are used to restrain a mare, kicking is prevented but the hocks may be raised suddenly and injure the operator if he is standing too close to the rear quarters. A mare can be examined in stocks, around a stall partition, or by being backed up to a manger or several bales of hay or straw. If a mare is in stocks, the rear rope or board should be low so that if the mare drops her hind quarters suddenly the examiner's arm will not be injured. It may be desirable to bandage the mare's tail and have it held upward and to one side by an assistant so the long tail hair does not irritate the anus and rectum at the time the arm is inserted and the tail does not become soiled. A bland, nonirritating lubricant should be used on the arm. The rectum of the mare is drier than that of the cow and the operator's arm requires frequent liberal lubrication. The author favors a bucket of soapy water made with bland soap and applied to the arm with a sponge. Nonirritating obstetrical lubricants such as K-Y Jelly or a low-cost lubricant of 500 grams of Na carboxymethyl cellulose (Hercules) mixed with 8 gallons of water and 100 ml of chlorhexidine (Novalsan) as used at the Univ. of California^{57b} are also satisfactory. The preparation of this latter lubricant requires careful control of temperature and mixing procedures. The peristaltic waves in the mare are stronger than in a cow. The hand and arm should be withdrawn from the rectum when a peristaltic contraction occurs. Trauma to the rectum is more easily produced than in the cow and has more serious and sometimes fatal consequences because of the mare's increased susceptibility to peritonitis. Lacerations of the rectum have become a serious malpractice problem not limited to younger inexperienced veterinarians. Of 54 cases of rectal tears over 90 percent resulted in the death of the horse. Of a total of 720 equine malpractice cases from 1968 to 1981 these rectal lacerations represented 13.4 percent.⁵⁰ The need for prompt vigorous surgical treatment of such tears of the rectum is imperative.^{57b} Even with such treatment the prognosis is guarded to poor. Rectal examinations should therefore

be made with quiet restraint, care, and gentleness. Daily or every other day palpation of the mare's genital tract and ovaries during estrus, especially by inexperienced operators to detect a mature follicle and predict the time of ovulation, caused a delayed and lowered conception rate.⁵⁶

After entering the rectum of the mare and locating the bony pelvis, it is easier to locate one of the ovaries, until with more experience the uterus can be readily found. The distinct fibrous bean-shaped ovary, 4 to 8 cm. long by 3 to 5 cm., in thickness is located about 10 to 20 cm. cranial to the shaft of the ilium and about 5 to 10 cm. below the lumbar vertebrae in the nonpregnant mare or mare in early pregnancy. The operator who uses his right hand can more readily locate the left ovary of the mare and vice versa. After locating one ovary the hand is passed down the proper ligament of the ovary to the uterus. The uterus is cupped in the hand between the fingers and thumb and palpation of the cranial border, ventral, and dorsal portions of the nonpregnant or early pregnant uterine horns, the opposite ligament and the opposite ovary is performed. The nonpregnant completely-involuted uterus during estrus or/aneustrus is pliable, soft, flat, and rather flaccid, 4 to 7 cm. wide and 2 to 5 cm., thick. In the maiden or young mare the nonpregnant uterus is suspended above the floor of the pelvis and abdomen. In older mares, especially the first month after foaling, the uterus may be located more ventrally and be hanging cranial to the pelvis in the abdominal cavity. In circumstances where the uterus was located well-forward and downward in the abdominal cavity, traction on the broad ligament, or bimanual examination, with the other hand in the vagina grasping and exerting traction on the cervix, could be helpful.²⁰

Uterine changes during pregnancy. A presumptive diagnosis of pregnancy may be made at 18 to 22 days after service by the absence of signs of estrus in a mare with a normal behavioral pattern. On rectal palpation at this time the uterus is firm and tubular, the cervix is also contracted and firm, and 1 or 2 follicles of small to medium size may be present in the ovaries. Possibly a thinning of the uterine wall usually near the bifurcation over the conceptus often can be palpated. The accuracy of rectal palpation at this time varied from 80 to 93 percent.^{5,26,35,48,52} These signs, together with those revealed by a speculum, of a pale rather dry vaginal mucosa and a closed, nonedematous external cervical os are highly indicative of pregnancy. Confirmation of this presumptive diagnosis should be performed by rectal palpation, and/or biologic tests for pregnancy at 30 to 45 and 90 days after service.

In most mares rectal palpation of the uterus to diag-

nose pregnancy can be performed by an experienced operator with accuracy from 30 to 40 days of gestation. Diagnosis usually is easier for the less experienced veterinarian from 40 to 50 days of pregnancy. Pregnancy diagnosis is easier in maiden mares or primigravidae, and barren, nonfoaling mares than in mares conceiving on foal estrus when the uterus has not completely involuted. Highly skilled veterinarians may accurately diagnose pregnancy as early as 20 to 30 days of gestation. Care must be used not to injure the embryo, the chorionic or blastodermic vesicle or the rectum.

Careful repeated early pregnancy examinations by rectal palpation of the uterus were not detrimental to fertility by causing an increased abortion rate.^{7,30,56,57} The rectal examination for the diagnosis of early pregnancy in mares consists mainly of gentle palpation of the oval chorionic vesicle in a localized area of the uterine horn and doesn't involve the procedures of direct palpation of the amniotic vesicle and manual slipping of the membranes as practiced in the cow. This may account for the much lower incidence of embryonic damage after rectal palpation in the mare. It is often desirable to reexamine the mare once or twice at 60 to 120 days of gestation to make certain embryonic death and resorption did not occur.

In the mare, as in the cow, early embryonic deaths are not uncommon with an incidence of 2 to 20 percent or greater between early pregnancy diagnosis and 110 days of gestation.^{11,42,46,60} A survey of 100 equine practitioners revealed that 5 to 6 percent of mares abort after having been diagnosed pregnant early in gestation.³¹ Early embryonic deaths with absorptions or probably abortions from 25 to 30 days of gestation was reported in mares on a low plane of nutrition.⁵³ In a preliminary study using ultrasound to diagnose pregnancy and early equine embryonic deaths from 20 to 50 days of gestation, embryonic deaths occurred at all intervals with peaks around 20 and 35 days.^{56a} The cause of the deaths was not determined. "Spurious" conceptions may follow a normal service in a healthy cycling mare in which further estrous cycles are not exhibited on regular teasing, and on rectal examination at a later date the mare is not pregnant. Some of these are undoubtedly due to early embryonic death, resorption, unobserved abortion or persistence of the corpus luteum. In a few instances one of a pair of twin embryos in mares may die early, the dead embryo and its membranes may undergo maceration and absorption of mummification and the normal embryo survives to term.

The thickness and tone of the uterine wall increases slightly in both pregnant and nonpregnant mares from days 10 to 16 after the onset of the estrus. From day

Table 4. Size and Characteristics of the Equine Fetus and Uterus During Pregnancy*

Days of Gestation	Size and Shape of the Chorionic Vesicle	Amount of Fetal Fluids in ml.	Diameter of the Horn Containing the Fetus	Weight of the Fetus	Length of the Fetus (C-R)	Fetal and Placental Characteristics
16	2-4.0 cm. Bantam's egg (round)				0.32 cm.	
20	2.5-4.5 cm. Small Hen's egg (slightly oval)				0.66 cm.	
25	2.5-4.5 cm. Small Hen's egg (slightly oval)	30-40			0.6-0.85 cm.	
30	2.5-5.0 cm. Hen's egg (oval)	40-50	4-1/2-5 cm.	0.2 gm.	0.9-1.0 cm.	Eye, mouth and limb buds visible, chorionic vesicle present only in the uterine horn.
35	3.5-6.5 cm. Goose's egg (oval)	60-90	4.5-6.5 cm.	0.8 gm.	1.5-2.0 cm.	
40	4.5-7.5 cm. Small orange (oval)	100-150	7-8.5 cm.	1.6 gm.	2.5-4.0 cm.	Eyelids and pinnae have appeared.
45	6-10 cm. Large orange (oval)	150-200	7.5-10 cm.	3.0-4.0 gm.	2.6-4.5 cm.	
50	12 × 7.5 cm. Small melon (oval)	200-350	8.3-10 cm.	5.5-6.5 gm.	3.0-6.0 cm.	
60	13.3 × 8.9 cm. Melon (oval)	300-500	8.9-10 cm.	10-20 gm.	4-7.5 cm.	Lips, nostrils, and beginning development of feet observed, eyelid partially closed. Placenta not attached but beginning to go into the body of uterus.
90	14 × 23 cm. Football (oval)	1200-3000	12.5-15 cm.	100-180 gm.	10-14 cm.	Villi of placenta present but without firm attachment, mammary nipples and hoofs visible, body and horn of uterus both involved and enlarged.
120		3000-4000		700-1000 gm.	15-25 cm.	External genitalia formed but scrotum is empty, placenta attached, ergots and orbital areas prominent.
150		5000-8000		1500-3000 gm.	25-37 cm.	May or may not have fine hair on orbital arch and tip of tail, prepuce not yet developed.
180		6000-10,000		3-5 Kg.	35-60 cm.	Hair on lips, orbital arch, nose, eyelashes and fine hair on mane.
210		6000-10,000		7-10 Kg.	55-70 cm.	Hair on lips, nose, eyebrow, eyelids, edge of ear, tip of tail, back and mane.
240		6000-12,000		12-18 Kg.	60-80 cm.	Hair on mane and tail, back and distal portion of extremities.
270		8000-12,000		20-27 Kg.	80-90 cm.	Short fine hair over entire body.
300		10,000-20,000		25-40 Kg.	70-130 cm.	Body completely covered with short hair, prepuce developed, hair in mane and tail increased.
330		10,000-20,000		30-50 Kg.	100-150 cm.	Complete hair coat and hair coat gets its final color, testes descend.

*1c, 4, 9, 10, 18, 20, 21, 23b, 36, 44b, 52, 54, 55, 59, 60.

16 to 21 there is a 3-fold increase in thickness in the uterine wall in pregnant mares while in nonpregnant mares the thickness of the uterine wall declines to a low point at the onset of the next estrum. The tone of the uterine wall follows the same pattern, with a definite increase in the tone of the uterine wall of both the pregnant and nonpregnant mares to day 16 followed by a decline in tone in nonpregnant mares to a soft flaccid state about one day before the next estrum. In pregnant mares the uterine tone continues to increase after day 16 with the uterine horn becoming round and tubular about 5 days later.^{7,26,35,43,44a,b,52}

Palpation of the chorionic or blastodermic vesicle.

During early pregnancy a portion of the uterine horn enlarges. (See Table 4). The earliest this can ordinarily be detected is 20 to 30 days. This enlargement is characterized by a circumscribed, **ventral** bulge or distention and thinning of the uterine horn just to the right or left of the center or bifurcation of the horns. The enlargement of the uterus produced by the ovoid conceptus in mares is localized and not diffuse as it is in the cow that has an elongated blastodermic vesicle. Rarely the embryo and its membranes may develop more laterally in either horn or in the body of the uterus. The spherical bulge or swelling is caused by the chorionic or blastodermic vesicle in early gestation and later by the oval chorioallantoic vesicle containing the enclosed amniotic sac and embryo, the vitelline or yolk sac and the allantoic sac. From 3 to 6 weeks the vitelline or yolk sac is large and the amniotic cavity around the embryo is small. The allantoic cavity grows rapidly from 5 to 7 weeks of gestation when it contains much fluid.^{22,55} This chorionic vesicle at first is oval and then as it enlarges it assumes a more ovoid, tubular or sausage-shaped outline and extends into the body of the uterus about 60 to 90 days of gestation. The uterine wall during this early stage of pregnancy is more tubular in shape, has a more tonic, firm consistency, and is thinner, especially over the ventral bulge. As in the cow these changes are primarily due to the localized distension of the uterine horn and body with fetal membranes and fluid, imparting the feeling of heavy, water-filled rubber balloon.

By 60 to 70 days the chorioallantoic vesicle is so large it is difficult to delineate its extent and the early uterine tonus is less evident. Slipping of the fetal membranes is not performed in the mare because it is difficult, possibly damaging to the embryo and not necessary because the discrete, localized oval area of the uterus occupied by the conceptus in early pregnancy readily differentiates pregnancy from pyometra or mucometra. The thicker, more tonic, equine rectal wall also makes this technique hazardous.

Palpation of the changes in the size of the horn and body containing the fetus has been outlined in Table 4. Since the size of the round and later oval chorionic or chorioallantoic vesicle is closely correlated with the size of the uterine horn, the diagnosis and duration of early pregnancy may be ascertained.

The pregnant uterus in the mare is usually suspended above or on the level of the floor of the pelvis until the third to fourth month of gestation, when it drops enough to rest on the abdominal floor and the ventral surface of the uterus can't be palpated. In older mares it may rest there by the third month. If the mare is more than 3 months pregnant it will be difficult or impossible to retract the uterus, due to its weight; whereas if the mare is not pregnant the uterus can be retracted and palpated. By the fifth to sixth month of pregnancy the uterus is well-forward in the abdominal cavity and the broad ligament is under definite tension. The ovary may be 20 to 25 cm. below the lumbar vertebrae and is moved with difficulty because of the stretching of the mesovarium.

Palpation of the fetus through the rectal wall can usually be performed from 90 to 120 days of gestation when the fetus feels like a small, heavy, submerged but floating object as the hand by a patting motion ballots it. It is usually possible in most mares to palpate the fetus per rectum from the third month throughout the rest of the gestation period. The size and weight of the equine fetus during the various stages of pregnancy are noted in Table 4. In a few deep-bodied older mares palpation of the fetus may be difficult from the fifth to seventh month of gestation. In these mares the location of the uterus, the position of the ovaries, and the palpation of

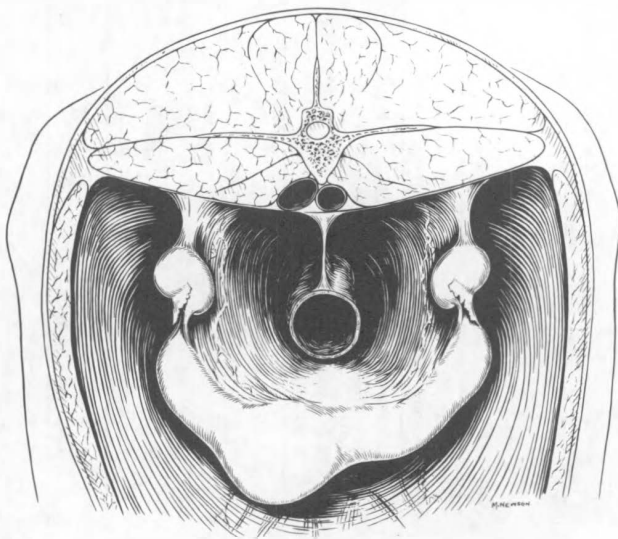


Figure 15. Uterus of a mare, 60 days pregnant.

the enlarged, whirring uterine artery will aid or confirm a diagnosis of pregnancy.

The ovaries of the mare during early pregnancy, differing from the cow, are of no value in determining the uterine horn containing the fetus. The corpus luteum is only palpable for a few days to a week after ovulation before it is covered by the dense fibrous ovarian tunic. A number of reports indicate that the incidence of ovulation may be slightly higher from the left ovary, 51 to 60 percent. The early embryo, up to 30 or possibly more days of gestation can migrate within the uterus resulting in slightly more pregnancies, up to 60 percent, in the right horn.^{1,3,8,13,25,38}

The gestation period can be divided into four periods based on the changes that occur in the ovaries.¹⁹ The first period, from ovulation to 40 days, is characterized by the presence of a single corpus luteum of pregnancy and a number of various-sized follicles on both ovaries. Great follicular activity occurs between 17 and 30 days after conception and before the secretion of gonadotropin by the endometrial cups.^{6,19,52} The second period, from 40 to 150 days, is characterized by marked ovarian activity many follicles over 1 cm. in diameter and the formation of accessory corpora lutea. Ovulation occurs during this period.³ Usually 3 to 5 or more accessory corpora lutea are present in each ovary. This ovarian activity with follicle and corpora lutea formation is probably caused by the high FSH and LH levels in the mare and not the high PMSG secreted by the endometrial cups from 40 to 120 days of gestation. Mares' ovaries apparently are unresponsive to PMSG (pregnant mare serum gonadotropin). The third period, from 150 to 210 days, is characterized by a regression of the corpora lutea and the absence of large follicles. The fourth period from 210 days to foaling no corpora lutea or follicles are present. During these latter two periods, gestation is maintained by steroid hormones produced in the placenta.⁴⁷

The vaginal examination as an aid in pregnancy diagnosis may be helpful but is not as accurate as the rectal examination of the uterus. By 30 days of pregnancy the normal equine vagina and cervix, on examination with a speculum, are very white and pale. They are more white and pale than at any time during the estrual cycle and resembles a mare's vagina in anestrus during the winter months. The mucous membrane is very dry, sticky, and gummy. There is less tendency for the vagina to balloon when the speculum is inserted than during the estrual cycle. More gummy mucus is present on the mucous membrane of the vagina during pregnancy than during the anestrus period. About 75 percent of pregnant mares show these characteristic vaginal changes.²⁰ The other pregnant mares may show a more hyperemic or con-

gested mucous membrane with less mucus. In rare cases a vaginitis with a mucopurulent exudate may be seen. The cervix in pregnant mares is usually tightly closed and small with a puckered external os. It is usually pulled downward and to one side. The external os of the cervix usually becomes covered with gummy, sticky mucus. In advanced pregnancy it may be easier to palpate the fetus through the vagina than through the rectum, as the mare objects less to the vaginal examination.

Differential diagnosis in pregnancy examinations should be considered by the inexperienced examiner. Occasionally a large endometrial cyst or lymph lacuna of the uterine wall may be mistaken for early pregnancy. From 70 to 110 days a distended bladder may be confused with pregnancy. Pneumovagina or a uterus filled with air might be mistaken for pregnancy. From 90 to 120 days an enlarged or distended right colon or pelvic flexure of the colon might rarely be confused with a pregnant uterus. Pyometra and mucometra associated with endometritis and focal cystic degeneration of the endometrium are occasionally found in the mare. The uterine wall and the fluid contents of the uterus may be heavy and thick. Tumors of the uterus and ovaries are uncommon in the mare. Mummification of a single fetus has not been observed in the mare. Fetal maceration is also uncommon.

Double ovulation occurs in 18 to 25 percent of mares and twin pregnancies are quite commonly diagnosed. But the incidence of twin births is low, 0.5 percent, due to embryonic or fetal death and abortion of possible of one, or more often, both fetuses.^{4,38} Twin embryos may be detected early, 21 to 25 days, by the palpation of two chorioallantoic vesicles or ventral bulges, often with one in each horn. If both vesicles lie close together producing a ventral bulge of the horn 10 to 30 percent greater in size than that of a single pregnancy, diagnosis is difficult, especially after 60 days.³⁵ Later, twin fetuses might be palpated and both uterine arteries might be enlarged.

Embryonic deaths in mares may be diagnosed at 35 to 45 days or more of gestation by a loss of fluid and tone in the chorioallantoic vesicle and a marked reduction in the size of the ventral bulge. These affected mares may not return to estrus and a regular estrous cycle for 40 to 80 days or more because of the presence of endometrial cups and the elevated secretion of PMSG.^{1,2,53} Douching the uterus with 500 ml. of warm saline or an injection of 10–15 mg. of prostaglandin (PGF_{2a}) or a prostaglandin analogue if performed before 40 days of gestation, usually results in a return to estrus within a few days in these mares. If early embryonic death is suspected, repeated examinations per rectum may be needed to confirm it.

The Biologic Tests for Pregnancy in the Mare

The tests are practical and nearly as accurate as pregnancy diagnosis per rectum. They are particularly indicated in highly nervous or vicious mares and small ponies in which rectal examinations would be highly dangerous for the operator or impossible because of the size of the animal. Veterinarians not experienced in the techniques of pregnancy diagnosis per rectum frequently employ these tests. The gonadotropic hormone, present at high levels during the early stages of the equine gestation period, is the principal hormone utilized for pregnancy testing.

The gonadotropic hormone (pregnant mare serum gonadotropin (PMSG) or equine chorionic gonadotropin, (ECG) from the endometrial cups in pregnant mares is first found in mare serum from 38 to 42 days of gestation. It reaches its maximum levels between 50 and 80 days and then gradually declines and is absent after 120 to 150 days. Ten ml. of blood should be drawn from the mare's jugular vein into a sterile tube. After clotting and separation of the serum at room temperature, the serum should be removed and refrigerated. Overheating of the sample should be avoided. This test may be conducted with accuracy from 40 to 120 days of pregnancy. Tests before 40 days and after 120 days of gestation in the mare may be inaccurate due to the low level of circulating gonadotropins in the plasma.

The hemagglutination-inhibition test is highly accurate, over 90 percent, in mares.^{14,32,41,49} The hemagglutination inhibition test utilizes the principle that PMS gonadotropins inhibit the agglutination of horse erythrocytes coated with PMS gonadotropin in the presence of PMS gonadotropin antiserum. This test, the Mare Immunological Pregnancy (MIP) test is sold commercially in the U.S. by Diamond Laboratories, Des Moines, Iowa. A recently developed radioreceptor assay test^{22b} and the possible commercial development of an ELISA test^{56a} for the presence of PMSG or ECG may be more accurate than the MIP test at 35 to 45 days to 100 to 150 days of gestation. Further studies should be conducted on these promising tests even though the former requires carefully controlled laboratory techniques.

The tests for gonadotropic hormone in pregnant mare serum are based on the development of endometrial cups in the region of the junction of the horn containing the embryo and the body of the uterus at about 30 to 40 days of gestation. These endometrial outgrowths are closely invested by the chorioallantois. The endometrial cups enlarge and fill with a mucoprotein secretion very rich in gonadotropic hormone the amount of which parallels levels in the blood.¹⁵⁻¹⁸ At 40, 80 and 150 days of gestation the total gonadotropic secretory activity in the cups

and in the plasma of the mare were 21,000 I.U. and 0.1 to 6.0 I.U./ml.; 73,000 I.U. and 6 to 296 I.U./ml.; and 42,000 I.U. and less than 0.5 to 106 I.U./ml., respectively. The equine gonadotropin produced in the endometrial cups is formed by the apocrine glandlike cells from the early chorionic girdle. The endometrial cups and their associated structures begin to show very early desquamation and regression at about 80 days of gestation and have completely desquamated by 100 to 120 days²¹ but the high levels in the plasma of PMSG may require more time to completely disappear.

When a mare is carrying a mule fetus the MIP test is not accurate because the equine gonadotropin concentration of her serum is about one-tenth that associated with a horse fetus.¹⁶ Ponies have as much as 8 times the concentration of gonadotropin as the draft breeds.¹⁷ This might be a breed difference or due to a dilution factor. Mares with a twin pregnancy of 52 to 72 days duration usually had twice the level of gonadotropin in their plasma than mares carrying single fetuses.⁴⁵ This difference was apparently due to a double set of endometrial cups in mares carrying twins. Ovarian activity was not correlated to gonadotropin levels in the blood. Gonadotropins are not found in the urine of pregnant mares as they are in women.

False negative reactions may occur due to taking serum from mares at 35 to 38 days and from 110 to 150 days of gestation when the level of serum gonadotropin may be very low in some mares. False positive reactions in mares may be due to early embryonic deaths that may occur in 5 to 10 percent of mares between 40 and 120 days of gestation and in which PMSG is continued to be secreted by the endometrial cups.⁴¹ Because of these occasional false positive results when testing for equine gonadotropin, some owners rely on the rectal examination or ultrasonography by a skilled veterinary examiner for the most accurate determination of pregnancy in mares.

Pregnant mares in which spontaneous or induced embryonic deaths occur after 40 days of gestation, when endometrial cups secreting PMSG are present, enter a pseudopregnant or infertile period that persists until the endometrial cups have sloughed or desquamated and levels of PMSG have disappeared from the blood plasma at about 120 or more days after conception. Thoroughbred mares during this period are in anestrus and have small firm inactive ovaries while pony mares have irregular frequent but anovulatory estrus periods characterized by follicular activity and apparent premature luteinization of the follicles. Repeated douching of the uterus or injections of prostaglandins to cause involution of the corpora lutea failed to produce estrus, ovulation and conception in these mares.^{1,2}

Other tests for gonadotropin in the plasma of mares

include the Ascheim-Zondek or immature rat test, the Friedman modification of the A.Z. test or rabbit test, the male frog or toad test and the direct latex agglutination test. These tests are more difficult, costly and give slower results than the convenient, practical, rapid, cheaper hemagglutination-inhibition or MIP test.⁴³ The Cole-Hart modification of the A.Z. test or "mouse" test is currently considered to be more accurate than the M.I.P. test or manual pregnancy test in mares for insurance purposes in Australia.^{39b}

The Cuboni and other tests for detecting the presence of estrogenic hormone in the urine of pregnant mares are accurate when applied from 120 to 250 days of pregnancy.⁴³ These tests have not proven practical because horse owners want the results of pregnancy testing much earlier than 120 days of gestation.

Pregnancy Diagnosis in the Ewe and Doe

Pregnancy diagnosis in the ewe and doe has been based primarily on post-conception clinical observations of changes in the animal similar to those occurring in the cow and mare, such as: service by a male and cessation of the estrous cycle. The use of a marking harness on the ram with different colored chalk used every 2 to 3 weeks and keeping of breeding records with ewe identification is desirable.^{8,12,17} In a well-managed flock over 90 percent of the ewes were marked and apparently bred but 20 percent failed to lamb so embryonic death losses probably occur. In advanced pregnancy there is an increase in the size of the abdomen and udder. The latter is most evident in primipara. During gestation up to 20 to 30 percent of pregnant ewes exhibit an estrous period of about 18 hours' duration one or more times. These periods were most common during early pregnancy but also occurred even in the late stages of gestation.^{8,22} Ninety-four percent of ewes failing to return to estrus by 21 days after service were pregnant but matings must be closely supervised and observations recorded.^{8,17}

In the ewe and doe one can occasionally observe **fetal movements** in advanced pregnancy and **ballot the fetus** on the right side from 3-1/2 to 4 months of pregnancy to term. The latter is most readily accomplished in thin fine-wool breeds by placing them on their rump on a crate and ballotting of the lower abdomen.^{7,15,18,21}

A radiographic diagnosis of single or possibly twin pregnancy can be made in 90 percent of ewes and does from 75 to 90 days of gestation to term but it is rather expensive.^{7,17}

The use of the **fetal electrocardiogram** as reported in horses and cattle has not proven practical for pregnancy diagnosis in sheep and does.^{7,17} The use of an **ultrasonic Doppler instrument** by rectal insertion or application to

the abdomen was over 90 percent accurate in the detection of pregnancy in ewes and does from 65 to 135 days of gestation.^{3b,4,7,9,10a,10b,12,13,17} These Doppler instruments detect movements of the fetus, blood in the heart and the pulse in the large vessels of the fetus. The accuracy in detecting twins was about 50 to 60 percent. Using an ultrasonic device similar to that used in swine had an accuracy of 80 to 90 percent in does and ewes pregnant more than 65 days.^{1a} (See Pregnancy Diagnosis in the Mare)

A direct method of palpation of the uterus with the fingers through a small abdominal incision in the inguinal region between 5 to 8 weeks of gestation was described.⁸ **Progesterone levels in blood** plasma, milk or milk fat may be used in ewes and does, especially the latter for pregnancy diagnosis. Blood or milk samples taken at 16 to 21 days and 32 to 35 days after mating in ewes and 21 days in does are analyzed by radioimmunoassay. Progesterone levels in blood and milk fat were more accurate for pregnancy diagnosis in does than milk levels.^{1c} High levels of progesterone indicate pregnancy and low levels nonpregnancy. The results are about 90 or more percent accurate when correlated with lambing of kidding.^{3b,7,12,14,17,20}

A bimanual rectal probe-abdominal palpation technique for ewes has been described and illustrated that is over 90 percent accurate by 65 to 70 days post-breeding. It is simple, easy and practical. Thin and relaxes ewes are easier to examine than fat or straining ewes. This technique was quite accurate in diagnosing single or twin fetuses.^{5,6,19} However, careful manipulation of the rectal probe is essential to avoid injury. Occasional abortions and deaths due to laceration of the rectum have been reported. Skilled operators produced very few rectal perforations but rectal abrasion and bruising are common, especially in nonpregnant ewes. This rectal abdominal palpation technique has been evaluated in does and is accurate⁸ but the possibility of abortions and deaths occasionally produced by this procedure limits its usefulness.¹³ **Laparoscopy or peritoneoscopy** with an instrument inserted through the upper right flank area is an alternative to the laparotomy procedure.^{3,11}

The technique of vaginal biopsy after 40 days of gestation was over 90 percent accurate for pregnancy diagnosis but was of no value in determining twinning. Its accuracy in detecting non-pregnant ewes was about 80 percent. This technique required a laboratory and a skilled person to examine the slides prepared from the biopsy of the vaginal mucosa.^{12,16}

A variety of other techniques to determine pregnancy in ewes and does have been evaluated, such as palpation of the caudal uterine artery per vaginum, assay of blood levels of estrogen and others but they are either unsat-

isfactory, unreliable, too expensive or too time consuming.^{7,12,17}

About 10 to 20 percent of the embryos in sheep, especially with double ovulation, will undergo transuterine migration from one horn to the other. Sixty-two percent of single ovulations in ewes and 56 percent of multiple ovulation occurred on the right ovary.¹ Ovine fetal crown-rump length at various stages of gestation are as follows: 30 days, 1.5 cm.; 60 days, 5.0 cm.; 90 days, 15 cm.; 120 days, 27 cm.; and 150 days, 50 cm.

Pregnancy Diagnosis in the Sow

Clinical observations may be used to diagnose pregnancy in sows as in ewes, cows and mares. Although the incidence of ovulation from each ovary may vary in sows, transuterine migration and placement of embryos results in nearly an equal number of fetuses in both uterine horns.^{3,13}

Rectal examinations and palpation of the uterine artery for diagnosing pregnancy can be performed in most sows and large gilts with an accuracy of over 90 percent after 40 or more days of gestation. Diagnosis was based on the size, tone and fremitus in the uterine artery compared to the external iliac artery. The tone of the cervix was also considered.^{1,8} Testing blood plasma for elevated **estrone levels by radioimmunoassay** between 20 to 30 days after service could be used as a pregnancy test in sows and gilts.^{3b,2,6,10,13b} This elevated estrogen level produced by the blastocysts in the uterus, was first detectable at 15 days after service and resulted in the maternal recognition of pregnancy and persistence of the corpora lutea. **Laparoscopy techniques** have also been used in sows and gilts for a highly accurate diagnosis of early pregnancy.¹⁶

Ultrasonography or ultrasonic amplitude depth or fetal pulse analysis, despite the initial cost of the equipment, is rapidly becoming the method of choice for pregnancy diagnosis in swine. A number of commercial companies are selling these solid-state machines utilizing a transducer probe placed on the lower abdomen or flank region of the female just lateral to the nipples and caudal to the navel and directed toward the uterus. A water soluble gel or corn oil is placed on the tip of the probe before placing it on the skin to improve contact. This test has proven to be over 90 percent accurate between 30 and 90 days of gestation in both pregnant and non-pregnant sows or gilts. The test is rapid and safe and restraint is minimal.^{3b,3,5,9} Amniotic and allantoic fluids are largely responsible for the positive acoustical patterns. The allantoic fluid increases rapidly from day 23 to day 65 and amniotic fluid from day 30 to day 80 of

gestation. The proportion of conceptus volume, fluids vs. fetus, declines rapidly after 90 days coinciding with rapid fetal growth resulting in a decline in the reliability of this method (amplitude-depth) after 90 days of gestation. The fetal-pulse ultrasonic analysis is over 90 percent accurate after 55 days of gestation.⁵

The **vaginal biopsy technique** for early pregnancy diagnosis in sows or gilts is over 90 percent accurate from 20 to 90 days after service. A special biopsy instrument is inserted into the vagina when the females are eating and a portion of the vaginal epithelium is recovered. Frozen, unstained tissue sections or stained tissue sections are examined under a microscope. A pregnant animal has four or fewer layers of epithelial cells with no interpapillary pegs. While a nonpregnant female has a many layered vaginal epithelium with abundant interpapillary pegs.^{3,4,5,7,15}

The fetal crown-rump length of swine fetuses at various stages of gestation is: 30 days, 1.8 to 2.5 cm.; 60 days, 8 to 11 cm.; 90 days, 17 to 23 cm. and at farrowing, 23 to 29 cm.¹⁴

Pregnancy Diagnosis in the Bitch and Queen

During pregnancy in the bitch there is usually a marked progressive increase in abdominal size from 35 days to term due to the deposition of fat and the increase in size and weight of the uterus. The teats between 35 to 45 days of gestation become enlarged and turgid. After 45 days they soften and become still larger. The mammary glands become enlarged and edematous from 50 to 55 days of pregnancy. Since these changes are even present, but usually less apparent, in non-pregnant bitches following estrus due to the pseudopregnant state, one must be cautious in diagnosing pregnancy on the basis of the above signs. Pseudopregnancy in the bitch extends for approximately the same period of time as gestation and may be followed by lactation if suckling is allowed. In dogs abdominal distention may also result from ascites, splenic enlargement, abdominal tumors, pyometra, or other causes.

Palpation of the uterus through the abdominal wall is one of the best and earliest methods of diagnosing early pregnancy in the bitch.¹ The ease with which this is done will depend on a number of factors such as: the temperament of the bitch, size of the dog, the stage of gestation, the number of fetuses in the uterus, and the degree of obesity.¹ At 18 to 21 days the embryos and their chorioallantoic vesicles produce a series of round swellings about 1.25 cm. in diameter in the uterine horns which frequently may be difficult to palpate at this time through

the abdominal wall. From 28 to 32 days of pregnancy these round ping-pong ball-like swellings in the uterus are about 1.5 to 3.5 cm. in diameter and are usually readily palpable. After 30 days it is difficult to palpate the pregnant uterus since the swellings increase in size, elongate, become confluent, lose their tenseness and come to rest on the abdominal floor. In some cases abdominal enlargement is noticeable. At 40 days of gestation these uterine swellings are 5.4×8.1 cm. in pregnant bitches.⁵

It is easier to palpate the caudal portions of the uterus. Fecal material in the colon should not be confused with pregnancy. From 45 to 55 days of pregnancy the size of the uterine horns and fetuses increase rapidly. The caudal fetuses are about 7.5 cm. long in medium-sized bitches and may be palpated in thin bitches with a thin, relaxed abdominal wall. The horn, since it is greatly distended and elongated, is usually bent in the middle at the liver. The apical portion of the horn is bent caudal and lies lateral and dorsal to the cervical portion of the horn. From 55 to 63 days the size of the fetuses are such that they can readily be detected. Rectal palpation with the finger with the forequarters elevated often is successful if palpation through the abdominal wall is difficult. The crown-rump length of the canine fetus at various stages of gestation is: 21 days, 0.7 to 1.0 cm.; 30 days, 1.5 to 1.6 cm.; 40 days, 6.3 to 7.8 cm.; 50 days, 11 to 12 cm. and 60 days, 14 to 20 cm.^{6,12}

Radiography is a helpful diagnostic aid in the bitch and queen especially late in pregnancy since fetal bones calcify during the last 20 days of gestation.^{7,10} With careful technique and experience the introduction of air, 200 to 800 ml., depending on the size of the bitch, into the abdominal cavity producing pneumoperitoneum, may help delineate the swellings in the uterus as early as 30 to 35 days of pregnancy. In the feline fetus the radius and ulna at 41 days and the tibia, fibula, ilium, ischium and occipital bones at 43 days, metacarpals and metatarsals at 49 days, and the entire skeleton at 55 days is calcified and can be visualized radiographically.^{1,3,4} Radiographs prior to 25 days in bitch and queen should be avoided because teratologic effects may be produced in the embryos.

In the queen palpation of the implantation sites in the uterus through the thin abdominal wall is easier than in the bitch and possible from 14 to 25 days but best accomplished from 17 to 21 days of gestation when these sites are about 1 to 1.5 cm. in size and firm. The fingers and thumb are placed together through the abdomen beneath the transverse lumbar vertebrae. Slowly draw these ventrally feeling first the rectum and then the uterus. After this period the uterus enlarges rapidly, becomes much softer and doughy and is difficult to palpate. By 45 days

of gestation the abdomen has become enlarged in queens carrying four or more fetuses. This manual examination should be done carefully and gently at all stages of gestation to prevent possible death and abortion of the embryos or fetuses. Between days 45 and term, the fetus, especially the head, can be palpated.

Ultrasonography or ultrasound techniques have been utilized in pregnancy diagnosis in the bitch and queen from about 30 days of gestation to term.^{1a} It may also be used to detect fetal life in conditions in which radiography and auscultation of the fetal heart are difficult or not definitive. Further studies are needed to develop and make more practical this technique. Presently the cost of the equipment is nearly prohibitive. (See Pregnancy Diagnosis in the Mare.)

Laparoscopy has been developed and used for pregnancy diagnosis in the bitch and queen. It is accurate in early gestation from about day 15 to term.^{3,8}

Biologic tests for pregnancy diagnosis are not available in the bitch and queen. Vaginal cytology is also unreliable.^{3,10}

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Chapter III

GESTATION PERIOD—EMBRYOLOGY, FETAL MEMBRANES AND PLACENTA—TERATOLOGY

The gestation or pregnancy period is the period from fertilization or conception, to parturition or the birth of the young. During this period single cells divide and develop into highly organized individuals. This antenatal period is the least understood and probably one of the most important periods of life. There is a separate and distinct physiology of the fetus and placenta that is being intensively studied. The mortality rate of the ovum, embryo, or fetus during this period is much greater than for any other period of equal length after birth. Because they are usually unrecognized, early deaths of the fertilized ovum, or the early embryo, with resulting resorption or abortion, are often considered as sterility or infertility. The expulsion of a dead embryo or fetus that has reached recognizable size is called an abortion. The expulsion of a live fetus is called a birth. Until birth has occurred the viable bovine or equine fetus should not be called a calf or foal. The antenatal bovine individual or fetus, not a "calf," is present in the uterus and may be balloted through the abdominal or rectal wall. Dead fetuses, not "calves," may be aborted, or expelled at term. Calves are only born alive and the term "born dead" is improper. Through common usage the fetuses expelled dead at parturition in swine and some other species are called stillbirths. Those born before the end of the normal gestation period are spoken of as premature calves, foals, pups and etc.

The gestation period can roughly be divided into two parts, based on the size of the individual and the development of its tissues and organs. These two periods in the gestation period of the cow are:⁶⁴ **The period of the early embryo, ovum or blastula**—Presently the designation of the period of ovum or blastula has been dropped because as soon as fertilization occurs embryogenesis begins. Unfertilized ova die within a few hours after ovulation. This period of about 10 to 12 days in the cow extends from the time of fertilization, that usually occurs within a few hours after ovulation, to the development of the zygote's primitive fetal membranes in the uterus. The size of the ovum in domestic animals, not including the zona pellucida or granulosa cells, is

about 120 to 180 microns at the time of fertilization and the shedding of the second polar body. During this period, division or cleavage of the fertilized ovum progresses in the region of the ampullary—isthmic junction of the uterine tube to the morula stage characterized by the inner and outer cell masses totalling about 16 to 32 cells. The morula enters the uterus on day 3 after fertilization in the sow and days 4 to 6 in the other domestic animals. By 8 to 11 days after fertilization the zona pellucida has fragmented and a blastocyst has formed composed of the embryoblast or inner cell mass and trophoblast or outer cell mass and fluid, probably absorbed from the uterine cavity. By 11 days in the ewe and 12 days in the cow the blastocyst is about 1 and 1.5 mm. in diameter, respectively. Elongation of the blastocyst has not yet occurred. During this period defective embryos die and are absorbed. The corpus luteum is developing and producing progesterone, a hormone necessary for the growth and preparation of the endometrium, so a favorable environment for the embryo will be present in the uterus. (See Chapter 20 on Embryo Transfer.)

Period of the embryo and organogenesis—This period extends from 12 to 15 days to about 45 days of gestation in the cow, 11 to about 34 days in the ewe and probably about 12 to 55 to 60 days in the mare. During this period the major tissues, organs and systems of the body are formed and changes in body shape occur so that by the end of this period the species of the embryo is readily recognizable. This usually coincides with the development of the eyelids.⁵⁴ Starting at 12 days of gestation in the ewe and 14 days in the cow the trophoblast elongates very rapidly so by 14 days in the ewe and 17 days in the cow it is 10 cm. to 30 cm. in length, respectively and maternal recognition of pregnancy occurs. By 18 to 19 days of gestation in the cow the trophoblast may extend into the opposite horn.^{33,41,52} In the sow during this same period, 13 to 17 days, the lengthening of the trophoblast and the migrating and positioning of embryos in the uterus occurs. By 24 days of gestation the trophoblasts in the sow are about 24 cm. long.^{1,3} In the mare, bitch and queen the trophoblast or blasto-

dermic vesicle does not elongate but remains oval during this period causing a localized enlargement in the uterus helpful in early pregnancy diagnosis. In the cow the amnion is completely formed and closed and somites are forming by 20 days of gestation, by 22 days the heart is crudely formed and beating, by 25 days the neural tube is closed and 25 somites are present, the allantois is well developed, anterior limb buds are formed and eye and brain development are well advanced.

In the cow, as in other animals, attachment of the fetal membranes is a gradual process that begins with the formation of the first villi about 30 days of gestation and progresses to a primitive attachment of the chorioallantois to the endometrium in the caruncular areas about 33 to 36 days of gestation.^{32,33} In the ewe attachment begins at about 17 to 20 days and is well-developed by about 28 to 30 days.¹⁹ While in the mare, attachment is delayed until 70 to 90 days when villi develop on the chorion and project into crypts in the endometrium.⁸ In domestic animals the term attachment is preferred to the term implantation or nidation. Implantation refers to the process in humans and rodents where the zygote erodes, penetrates and implants itself within the endometrium. Up until the time of the well-developed attachment of the chorion to the endometrium the nourishment of the early embryo is provided by the secretion of the uterine glands called "uterine milk," a yellowish or whitish, thick, opaque secretion, grossly resembling, and occasionally mistaken for, a purulent exudate.

During this period nearly all of the more severe teratologic defects or anomalies of development occur. Also during this period the embryo may die, be expelled unnoticed at the next estrus, or become macerated and absorbed without external signs.

The period of the fetus and fetal growth. This period extends from about 34 days of gestation in the ewe and bitch, 45 days in cows and 55 days in the mare to parturition. During this period minor details in the differentiation of organs, tissues, and systems occur along with the growth and maturation of the antenatal individual. Changes in the bovine fetus from 70 days to parturition are not radical. During this period caruncles and cotyledons develop and enlarge to supply nutrition to the fetus in the cow and ewe. The increase in size of the fetus is a geometric-like curve, with the weight of the bovine and equine fetus increasing very rapidly the last two to three months of gestation.^{8,22,24,27} From 210 to 270 days the increase in weight of the bovine fetus is equal to three times the increase from the time of fertilization to 210 days.

The prenatal development of the ovine and bovine zygote have been carefully described.^{18,31,58,64} The em-

bryology of swine has been reviewed.⁶ Recent valuable information on embryology in horses and dogs, has been provided.^{8,22,25,27}

Embryology

Embryology is the study of the physiological development and growth of the antenatal individual. **Teratology** is the division of embryology and pathology dealing with abnormal development and malformations of the antenatal individual. Teratologic studies are of value because they constitute important available records of injury and arrested or pathologic development of the embryo or fetus. These studies explain the nature of some of the teratologic abnormalities in the fetus that frequently result in dystocia as well as other defects of the reproductive and other body systems. The embryology of importance in obstetrics, excluding that relating to the male and female reproductive systems which are discussed in detail elsewhere, is as follows:

The nervous system. The hypophysis or pituitary gland is an important endocrine gland. It is composed of the anterior, intermediate, and posterior lobes. The former and latter are of greatest significance. The posterior lobe arises embryologically as a downward extension of the floor of the diencephalon, a portion of the primitive brain. The deep portion of Rathke's pocket loses its original connection with the stomodeal ectoderm and becomes closely applied to the infundibulum and forms the anterior lobe. Thus the posterior lobe of the hypophysis arises from neural tissue and the anterior lobe from ectodermal tissue. Teratologic defects or arrests in development of the nervous system may result in such conditions as: ankyloses, hydrocephalus, hypoplasia of the cerebellum, cerebral hernia, cyclopia, lack of optic tissue, and persistence of the anterior neuropore with failure of facial bones to fuse (*Schistocephalus bifidus*).²

The digestive system. This system is of little importance in obstetrical studies in animals. Arrested development at the terminal portion of the digestive system may result in atresia ani or the lack of a rectum. Occasionally a common cloaca is observed in the female or atresia ani is made less acute by the rectum emptying its contents into the vulva. Anomalous development of the gut may result in atresia coli. In the mouth region arrested development may result in a cleft palate or persistence of epithelial linings of the pharyngeal pouches, as seen by pharyngeal cysts in dogs.

The circulatory system. The heart, arising from the fusion of the primitive endocardial tubes, develops initially in the neck region caudal to the gill clefts or pha-

ryngeal arches and then descends into and is enclosed by the chest in the bovine embryo around the fifth to sixth week of gestation. If this fails to occur the condition of ectopia cordis results. When the heart descends, the aortic arches descend also and carry with them the laryngeal nerves. The left aortic arch persists and the right aortic arch disappears. In dogs and cattle and rarely in other animals, the right aortic arch persists and the left disappears. In these instances, if the left ductus arteriosus is present, a chronic stenosis of the esophagus occurs as it passes over the base of the heart. It is compressed between the trachea, the aorta, the ligamentum or ductus arteriosus, and the base of the heart.

The fetal venous circulation of blood consists largely of "arterial" blood rich in oxygen and nutrients coming from the placenta into the umbilical vein of the fetus. This vein passes through the umbilicus into the liver of the fetus where it anastomoses with the portal vein. In the fetal liver in most animals including the dog, cow, and sheep there is a direct shunt, called the ductus venosus, from the umbilical vein to the posterior vena cava. The blood that enters the portal veins goes through the liver tissue and into the posterior vena cava by means of hepatic veins. From the posterior vena cava, the blood then enters the right atrium where about 50 percent of it is immediately shunted through the foramen ovale into the left atrium.²⁰ The remainder passes into the right ventricle and is pumped into the pulmonary artery, where again a large portion of the blood is shunted through the

short ductus arteriosus into the aorta. A small amount goes through the pulmonary artery into the lungs as only a small blood supply is needed since the lungs are not functional in the fetus. Blood from the lungs is returned to the left atrium by the pulmonary veins. Blood that comes through the foramen ovale is mixed in the left atrium with blood from the pulmonary veins, passes to the left ventricle, and is pumped into the aorta and thence through the arteries to the various organs and tissues of the body. The aorta carries blood caudally to the rear quarters and in the region of the last lumbar vertebrae the two large umbilical arteries arise that carry largely "venous" blood down on either side of the bladder through the umbilicus to the placenta where waste products and carbon dioxide can be exchanged for nutrients and oxygen. More than 50 percent of the fetal cardiac output goes to the placenta.²⁰ In the fetal lamb at 130 days of gestation 48 percent of the blood volume was in the placenta; at near term about 26 percent of the blood volume was in the placenta.^{5,6} The effect of allowing the cord to remain intact for a short time after birth to increase the blood volume in the newborn is evident. Hemoglobin values and red blood cell numbers in the fetus are much higher than in the adult. These values rapidly drop to normal after birth. Fetal hemoglobin apparently has a greater affinity for oxygen and releases it more slowly than does hemoglobin in the adult. The fetus has a high heart rate, about twice that of a young animal, promoting a high cardiac output per unit of body weight necessary

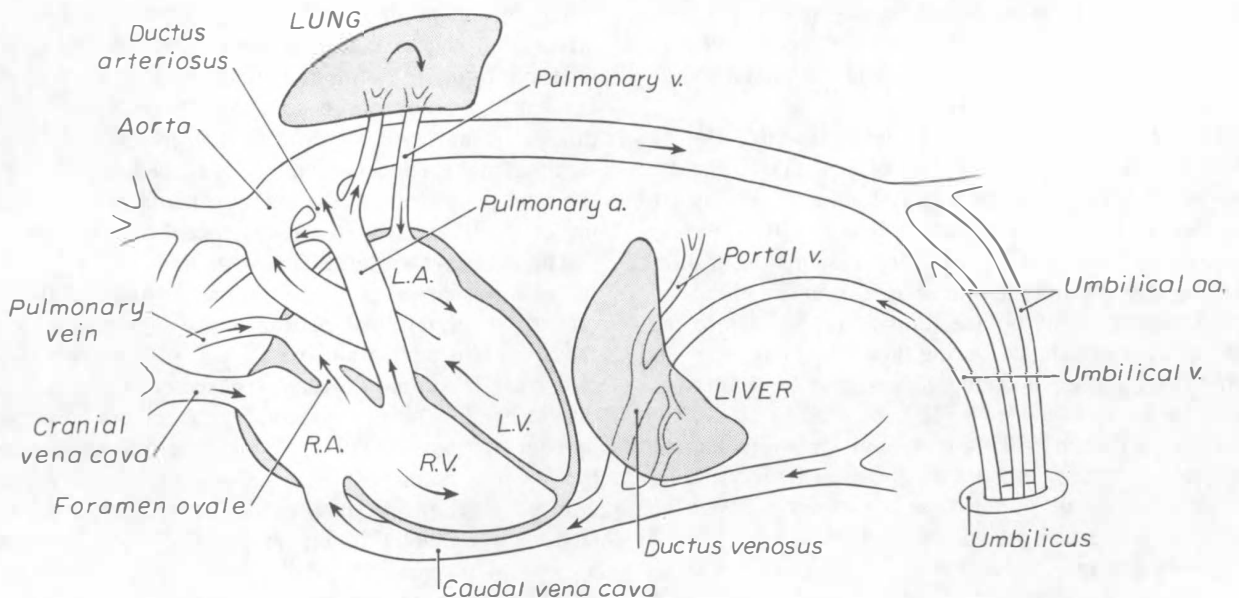


Figure 16. Diagram of fetal blood circulation (arrows indicate the direction of the blood flow).

to compensate for the low oxygen content of the fetal blood.^{5,6}

Marked changes occur in the fetal circulatory system at the time of birth.^{20,29} The umbilical cord ruptures. The umbilical vein present in the umbilical stump apparently closes due to a smooth muscle effect. The remnant of this vessel from the umbilicus to the liver becomes in later life the round ligament of the liver. The ductus venosus is apparently closed by a smooth muscle sphincter within 30 minutes to several hours after separation of the umbilical cord. In later life it becomes the ligamentum venosus in the substance of the liver. The liver then has the entire volume of portal blood going through its lobules instead of about one-third the volume. The foramen ovale closes mechanically within 5 to 20 minutes after birth by the closing of its lumen with the thin fold of tissue lying in close apposition to the foramen. This thin membrane or valve is maintained by an increase in blood pressure in the left atrium over the right. Finally after a year or more a complete septum is formed, the ductus arteriosus is closed by the contraction of its smooth muscle within 4 to 5 minutes after birth. This closure is apparently associated with an increased supply of oxygen in the blood of the newborn. The ductus arteriosus atrophies and eventually becomes the ligamentum arteriosum. The umbilical arteries are stretched at the time the cord is broken and they contract into the abdominal cavity and are closed by smooth muscle contraction. These are similarly affected by an increased oxygen level in the blood. The umbilical arteries later become the round or lateral ligaments of the bladder. Concomitant with these changes after separation of the fetus from the placenta at birth is a marked rise in arterial blood pressure.^{5,6} Defects in cardiac development are occasionally seen in animals, especially calves, dogs and pigs, where they may be associated with weakness, hypoxia, signs of circulatory failure, and death soon after birth.

The urinary system. This system is formed mainly from mesodermal tissue. The earliest or most primitive urinary or excretory organ in the embryo is the pronephros with two pronephric ducts, one on each side in the body wall dorsal to the peritoneum. This organ soon degenerates, to be succeeded by the mesonephros or Wolffian body. This structure, using the earlier pronephric ducts now called mesonephric or Wolffian ducts opens into the common cloaca. Later in the development of domestic animals the mesonephros degenerates and the metanephros or true kidney develops more caudally as an outpocketing of the mesonephric ducts. These ducts become the ureters, which open into the bladder. This latter structure opens caudally by the urethra into the amniotic cavity and cranially by the urachus into the allan-

toic cavity. During most of the late development of the fetus, urinary wastes are discharged principally into the allantoic cavity and little passes through the urethra into the amniotic cavity. Occasionally in domestic animals anomalies of the urinary system are observed, with polycystic kidneys or dilations or stenoses of the ureter. In rare cases a horse-shoe kidney, *ren arcuatus*, in which both kidneys are joined, is observed. This condition is noted more frequently in fetal monsters. The embryology of the genital system of the male and female animals are discussed separately in chapters relating to the anatomy of the genital tract.

The physiology of the fetus is a fascinating study. It has been shown that contractions of the heart and circulation of the blood through the vessels occurs early in the embryonic period. During this period respiratory movements are present. Although they may occur intermittently at first, they become more frequent and occur continually during the period of the fetus. The principal carbohydrate circulating in the ovine, caprine, equine, porcine and bovine fetuses is fructose produced by the placental tissues while in the canine and feline fetuses it is glucose.³⁶ Fructose does not pass through the placenta into the dam's circulation. The fetus starts swallowing late in the embryonic or early in the fetal period. Undoubtedly large amounts of amniotic fluid are swallowed and absorbed. Some of the waste products are stored in the rectum and colon as part of the meconium. This swallowing reflex of the fetus may be associated with maintaining the proper amounts of amniotic fluid. In fetal monsters, where defects of the cranial portion of the fetus or alimentary canal are present, hydrops amnii often occurs.

Fetal movements begin early, at 90 days in the mare, and are more or less continuous in the form of paddling movements of the limbs and moving of the head and neck.³⁰ If these movements do not occur or are markedly restricted, ankyloses with such abnormalities as wry neck or ankylosed limbs may result.

The Fetal Membranes and Placenta

The fetal or extra-embryonic membranes serve as protection, a means of transmitting nutrients from the dam to the fetus, in caring for fetal waste products and synthesis of enzymes and hormones. The latter are necessary for the maintenance of pregnancy in most domestic animals. The fetal membranes are discarded at the time of parturition. The fetal membranes consist of the primitive yolk sac, the amnion, the allantois and the trophoblast or chorion which when combined with the allantois

forms the chorioallantois. The trophoblast is the most important single tissue of the fetal membranes and placenta as it has functions of absorbing, transmitting and handling nutritive and waste products. It has an erosive action on the endometrium mediating the attachment of the blastocyst; and it has a regulating function by being the site of the synthesis of enzymes and hormones. The needs of the embryo and fetus are supplied and cared for as follows: water, oxygen, and nutrients are taken from the maternal structures as the uterus and, after placental attachment has occurred, the maternal blood and carried to the developing embryo and fetus by the yolk sac, the amniotic chorion and the chorioallantois. The first two structures develop early in the life of the embryo of domestic animals and only function a short period of several weeks until the chorioallantois develops. Waste products from the embryo and fetus such as carbon dioxide and urea are eliminated by the same structures. The allantoic cavity stores much waste material from the fetal kidneys. The large intestine and rectum of the fetus store waste products from the digestive tract as meconium. The amniotic cavity may play an early role in the care of some waste products. The fetal fluids permit the growth and movement of the fetus by distending the uterine lumen. Protection of the embryo and fetus is performed principally by the amnion, although the allantois, uterus, and maternal body assist in this function. Heat and immunity to early diseases of the newborn are supplied by the mother's body. These immune bodies in domestic animals are mainly supplied by the colostrum. The fetal membranes and placenta have been well-described.^{1,2,10-14,55,61,63}

The **yolk sac** is a primitive structure developing early in the embryonic period from the endoderm and disappearing after a short period of time in ruminants and swine but persisting for 4 to 6 weeks in the horse before becoming a remnant in the fetal membranes.^{11-14,60} Prior to the formation of the amnion, the blastocyst or blastodermic vesicle and then the yolk or vitelline sac perform limited placental functions of providing nutrients and care of waste for the early embryo. The endometrial or uterine glands, under the influence of progesterone from the corpus luteum, produce a secretion called "uterine milk." This contains protein, fat globules, organic and inorganic solids, and possibly other nutrients.^{5,1,2} This uterine secretion is absorbed by the blastocyst and yolk sac for the nutrition of the early embryo and later by the chorioallantois for the early fetus. Its role in middle or late gestation is probably not important.

The **amnion** forms about 13 to 16 days after conception in the ewe and cow, probably about the same time in the mare, and slightly earlier in the sow, bitch, and queen. The amnion is an ectodermic vesicle that arises

from an outfolding of the chorion, or from a space in the inner cell mass of the blastocyst, as a double-walled sac that completely surrounds the fetus except at the umbilical ring. When this sac is completed it is filled with amniotic fluid which surrounds the embryo and thus is a mechanical protection to the fetus. There is a thin sheet of smooth muscle in the amnion that contracts producing a tense amniotic vesicle.³⁵ Amniotic fluid also prevents adhesions between the soft, developing tissues of the embryo and the surrounding membranes which might cause malformations. The inner layer of this double-walled sac is the "true amnion" and the outer layer is the "false amnion," amniotic chorion, or portion of the trophoblast or serosa over the true amnion. Until the allantois is formed and the external portion of it fuses with the chorion, the amniotic chorion acts for a very short period, as did the yolk sac, in providing for the transfer of nutrients and for the care of wastes for the embryo.

The amnion during the fetal stage of development is a rather transparent, tough membrane. It provides the outer covering of the amniotic portion of the umbilical cord. On the inner surface of the bovine amnion are small, 0.25 to 1.5 cm, irregular-shaped, flat, white, elevated epithelial thickenings, called amniotic plaques. They are most noticeable during the third to seventh months of gestation. The portion of the amnion covering the cord of the bovine fetus is also covered with these amniotic plaques but at this site they are coarse, elongated villi or papillary elevations. They vary widely in number and consist of edematous epithelial cells that sometimes are keratinized. These amniotic proliferations are also found to a lesser degree in mares, ewes and does but not in sows and carnivores. The etiology or significance of these amniotic plaques is not known. They apparently are not due to infectious agents, either bacterial or viral. There are no inflammatory lesions associated with these plaques.⁴⁷

The amniotic fluid is clear, colorless, and mucoid in nature. This fluid is present toward the end of gestation in amounts of 2000 to 8000 ml. with an average of 5000 to 6000 ml. in the cow, 3000 to 7000 ml. in the mare, 400 to 1200 ml. in the doe, 350 to 700 ml. in the ewe, 40 to 200 ml. in the sow, and 8 to 30 ml. in the bitch and queen.^{1,2,3,5,7,15,65} Amniotic fluid contains the following substances: pepsin, a diastatic ferment, a lipolytic ferment, protein, fructose, fat, and salts. It is bactericidal and prevents adhesions.⁴⁶ Concentrated bovine amniotic fluid has been recommended for the prevention of peritoneal adhesions following abdominal operations in humans. Changes in the biochemical constituents of amniotic and allantoic fluids in cows during gestation has been reported.⁶⁶

The source of the amniotic fluid in early to midges-

tation is probably from the amniotic epithelium and from the fetal urine as the fluid is quite watery. As gestation advances the allantoic fluid increases in volume while the amniotic fluid volume remains fairly static but becomes viscid and glairy because the bladder sphincter prevents the further release of urine into the amniotic cavity. The probable source of the mucoid amniotic fluid is then the saliva and secretions of the nasopharynx of the fetus. The volume of amniotic fluid is probably partially regulated by swallowing by the fetus.^{3,5,6,61} The normal fetus does not inhale amniotic fluid into the lungs. The amniotic fluid aids parturition because its slippery, mucoid consistency lubricates the fetus and birth canal.

Pathologically, especially in fetal monsters or certain types of fetuses carried overtime, the amount of amniotic fluid may be greatly increased up to 8 to 10 times. This condition is called *hydrops amnii*. Another abnormal finding in the cow and ewe is the presence of meconium in the amniotic fluid causing staining and smearing of the fetus. This is probably caused by perinatal asphyxia or hypoxia.^{19b} In rare instances hairballs may be found in the amniotic fluid, especially in prolonged gestations associated with fetal giantism.

The **allantois** arises the second and third week of gestation in bovine fetuses as an outpocketing of the hind gut almost as soon as the hind gut is formed. The allantois consists of entoderm covered by a vascular layer of splanchnopleuric mesoderm. The outer layer of the allantois is eventually richly supplied with blood vessels connected to the aorta of the fetus by the umbilical arteries and to the liver and posterior vena cava by the umbilical vein. As the allantois grows and enlarges it extends between the true and false amnion. The outer layer of the allantois fuses with the trophoblast, false amnion, or serosa to form the chorioallantois. The inner layer, largely devoid of blood vessels, lies against the amnion and invests the allantoic portion of the umbilical cord. The allantoic sac or cavity is filled with allantoic fluid. The allantois is completely formed in the larger domestic animals by 24 to 28 days after conception and extends the entire length of the fetal membranes except the undilated apices of the chorionic or blastodermic vesicle in the ewe, sow, and cow. Because they are not supplied with blood vessels, these undilated apices atrophy and become necrotic and are called the necrotic tips of the chorioallantois. The small amount of allantoic fluid present before the fetal kidneys are active probably comes from the allantoic epithelium or by absorption from the uterine lumen. A precipitation of calcium in the allantois chorion causing white streaks or mottling is commonly observed from 60 to 90 days of gestation in the cow after which time it is removed and disappears as it is deposited in the fetal bones. A similar calcium storage in the

allantois chorion has been reported in pigs between 20 and 46 days of gestation.⁴³

The allantoic cavity stores the waste products of the fetal kidneys, which pass to it from the bladder through the umbilical cord by means of the urachus. This fluid is clear, watery, and amber in color and contains albumen, fructose, and urea. In a number of animals such as the sow and ewe the amount of allantoic fluid rises sharply during early pregnancy, rises more slowly around midpregnancy and then rises sharply toward the end of gestation. The allantoic fluid in the sow may decline the latter half of gestation.⁶⁵ In all animals the amounts of amniotic and allantoic fluids are variable.^{2,1,2,3,15,22,24,53} Toward the end of gestation the volume of allantoic fluid varies from 4000 to 15000 ml. averaging about 9500 ml. in the cow, from 8000 to 18,000 ml. in the mare, 500 to 1500 ml. in the ewe and doe, 100 to 200 ml. in the sow, 10 to 50 ml. in the bitch, and 3 to 15 ml. in the queen.

Occasionally excessive amounts of allantoic fluid, 40,000 to 160,000 ml. or more, may accumulate in the allantoic cavity. This condition is called *hydrops allantois*. This excessive fluid has the specific gravity and characteristics of a transudate. The cause is most commonly due to a vascular disturbance in the allantois.

Amorphous, semisolid, amber-colored, soft, pliable, rubber-like, irregular-shaped masses or bodies, thinner at the edges and thicker in the center, 2.5 to 15 cm. in diameter and from 0.3 to 3.8 cm. in thickness are commonly found in the allantoic cavity floating in the allantoic fluid of the cow, mare, ewe, doe and sow. These bodies are called *hippomanes* (after hippo or horse and manes or manus, Latin for hand) In a few cases these masses, resembling fibrin in appearance, have been observed fastened to a fold of the allantois. Hippomanes have been described as allantoic "calculi" consisting of a central nucleus of desquamated cell debris upon which were deposited in a concentric manner a denatured mucoprotein complex and minerals, mainly calcium phosphate.³⁸ This allantoic "calculus" has a higher specific gravity than allantoic fluid and if free-floating will sink to the bottom of the allantoic cavity. The author has not observed the reported concentric deposits in the formation of hippomanes and still considers their etiology an enigma. Occasionally the allantois will become pathologically thickened and edematous, edema of the allantois chorion.

The **chorioallantois** or **allantois chorion** is formed by the fusion of the outer layer of the vascular allantois and the trophoblast, chorion, or serosa. This structure, richly supplied with blood vessels communicating with the fetus and in intimate contact with the endometrium, is designed to carry on the metabolic interchanges of gases,

nutrients, and wastes between the fetal and maternal circulations. It actively begins this function with its formation and grows and develops as required by the needs of the fetus. The allantois chorion is the fetal placenta. Although liquids and gases may pass through the chorion to the maternal and fetal circulations, solids and most bacteria ordinarily cannot pass unless disease of the chorion is present. Certain bacteria, viruses, fungi, and parasitic larvae can penetrate the intact placental barrier.

In the cow, sow, and ewe the allantois is attached to the amnion at various points. This divides the allantois into a number of compartments. In the bitch, queen, and mare the amnion containing the fetus floats free in the allantoic cavity attached only by the umbilical stalk. In these latter animals the young are more apt to be born covered by the amnion or a portion of it. Unless it is promptly removed, they will smother if it lies over the nostrils and mouth. This rarely happens in the cow, sow, and ewe. The necrotic tips of the chorion, found at the apices of the chorioallantois, are observed in the ewe, cow, and sow, and are usually about 1 to 2.5 cm. long and about 0.3 cm. in diameter. In the mare an irregular bare spot in the diffuse placenta of the chorion is found over the internal os of the cervix and is called the "cervical star." Since the allantois chorion and endometrium are in intimate contact for most of the gestation period, disease or abnormalities of either is mirrored on the other. A careful examination of the fetal placenta after parturition will give an accurate index of the health of the uterine endometrium.

The Placenta

The placenta is composed of two parts: the fetal placenta, or allantois chorion, and the maternal placenta or endometrium. For a few weeks in the early embryonic period the yolk sac and amniotic chorion act as primitive placentae. During the first month or more of gestation, the blastocyst becomes attached to the endometrium, and the fetal membranes, including the allantois chorion, develop. At this time the villiform projections of the chorion and the maternal crypts in the endometrium, into which they extend, are rudimentary, small, and friable. During this early period in domestic animals much of the nutrients still are absorbed from the uterine secretions. Not until the end of the first third of gestation do the anatomical attachments of the maternal and fetal placentae become sufficiently intimate and complex to prevent the very easy separation of these two structures. Until this time the fetal membranes and embryo are held in place in the uterus by the accumulation of fluid within the membranes.

That a pregnant animal does not reject her placenta is an apparent biological paradox. With half of the genetic make-up of the fetus and placenta contributed by the sire there should be sufficient tissue incompatibility to induce an immune reaction in the dam and subsequent rejection of the conceptus. It has been postulated that the greater the trophoblastic invasiveness, as in man and rodents, the greater the necrosis of both chorionic and endometrial tissue.⁶⁶ This resulted in the development and deposition of a mechanical acellular barrier of acid mucopolysaccharide in those animals such as man and rats having a hemochorial placenta. In the epitheliochorial placentas of the mare, cow, sow, and ewe where the interdigitating microvilli of the chorion or trophoblast and endometrial epithelium are closely apposed, no extensive degeneration or deposition of fibrinoid is present. Therefore in the former an acellular mechanical barrier and in the latter the absence of trophoblastic antigenicity may offer reasonable explanations for retention of the placental homograft. The inability of immunologically active maternal cells to penetrate into the fetal circulation may also be important. Further immunological studies are needed to explain this failure of placental rejection.

Anatomically the placenta of animals may be divided into 4 general types based on their shape; the diffuse, the cotyledonary, the zonary, and the discoidal.

The diffuse type. In the mare and sow the entire surface of the allantois chorion is covered with microcotyledons, villi and microvilli that project into crypts or pockets in the endometrium. In the former these complex structures are completely formed by day 150 of gestation.⁵⁷ The entire endometrium and chorion take part in the placentation except over the openings of the uterine glands where the glandular secretion causes a separation of the two structures. These whitish structures are large and abundant in the pig placenta and are called areolae. In the mare the region of the internal os of the cervix is devoid of villi, the cervical star, as are occasional bare areas elsewhere due to placental folding. In the sow the apices or paraplacental zone of the placentas that abutt against the adjacent zone of the next placenta are free of villi and as pregnancy progresses the trophoblast and allantois in this area disappear and these areas fuse. The placental bed of each porcine fetus enlarges until nearly all of the endometrium is utilized.⁴ Uteroferrin, a glycoprotein, found in uterine secretions of sows and mares with a diffuse type of placenta is probably involved in iron transport to the embryo.⁶⁷

The cotyledonary or multiplex type. In ruminants, including the cow, ewe and doe, only a portion of the maternal placenta, or the endometrial caruncles, and portions of the allantois chorion, or cotyledons, which

closely appose each other to form the placentome, take part in the placental functions. In these structures the villi, secondary villi and microvilli of the cotyledon fit together closely with the maternal crypts and microvilli in a more complex arrangement than in the diffuse type of placenta. In the ruminant uterus the caruncles are arranged in 4 rows, 2 ventral and 2 dorsal, the length of each uterine horn. There are between 75 and 120 placentomes in the normal pregnant uterus of the cow, and about 80 to 90 in the ewe. Occasionally due to prior uterine disease or a failure of the horn opposite the one containing the fetus to form placental attachments, the numbers of placentomes may be reduced to one-half or less of the normal complement. In pregnant cows the convex uterine caruncle is elevated above the endometrium like a button, with the concave fetal cotyledon grasping it (See Figure 18). In the ewe and doe the maternal caruncle is also elevated above the endometrium but it is concave in shape, with the fetal cotyledon fitting into it (See Figure 17). The endometrium between the caruncles is called the intercaruncular endometrium and the fetal placenta between the cotyledons is called the intercotyledonary placenta. This area normally does not take part in placental functions once the placentomes are formed. Occasionally because of uterine disease or due to a lack of placentomes, primitive placental structures, simulating a diffuse placenta, develop in this area between the allantois chorion and the endometrium. These are called adventitious placentae, or "accessory placentomes."⁴¹ These may be few in number or they may involve a large portion of the intercaruncular endometrium and chorion. When these are extensive and numerous the pregnancy is usually insecure and the possibility of subsequent normal pregnancies questionable.

A confusion in nomenclature existed in the older American veterinary literature regarding the use of the term, cotyledon. American veterinarians formerly called the combined maternal and fetal placental structure palpated through the uterine wall of a pregnant bovine uterus

during a rectal examination as a cotyledon.⁷ Recent veterinary authorities stated that the cotyledon was the fetal placenta that produced villi which projected into the crypts of the maternal caruncle that had become greatly enlarged. These two structures, the maternal caruncle, and the fetal cotyledon in ruminants was termed a placentome. This latter nomenclature is preferred by the author.^{1,2,10-14}

The zonary type. In the bitch and queen the placenta forms a zonary band or girdle about 2.5 to 7.5 cm. in width around the circumference of the uterine lumen in the middle of the oval chorionic sac. It is a highly complex structure. In carnivores the placenta is of a labyrinthine, rather than a villous type that interlocks more intricately than does the maternal and fetal placentae in the larger domestic animals. The rest of the chorion is bare and devoid of villi and does not take part in placental functions during most of the gestation period. Placental hematomas or extravasations are observed as green and brown borders or margins of the zonary placenta in the bitch and queen, respectively. These are seen in the cow and ewe as multiple hematomas within the placentome at the base of the chorionic villi. They are considered to play an important role in the nutrition of the fetus because this stagnant maternal blood breaks down providing a source of iron that is utilized by the fetus.⁶³

The discoidal type. This type is not seen in domestic animals but is present in primates and rodents. There is a round to oval, disc-shaped placental area of the endometrium and allantois chorion. In these species the placental union is even more intricate and intimate than in the others.

Another method of classifying placental types is by the microscopic tissues, layers or structures that intervene between the maternal and fetal blood.^{1,2,34,48,63} The placentae of various animal species have recently been carefully examined with the electron microscope.^{10-14,66} Although the types of placentae were originally classified physiologically and anatomically, this classification

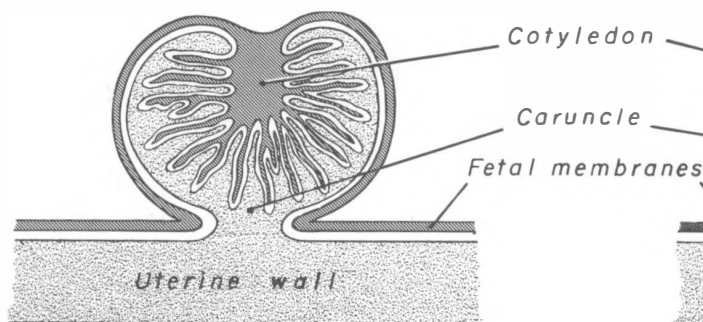


Figure 17. Placentome of the ewe.

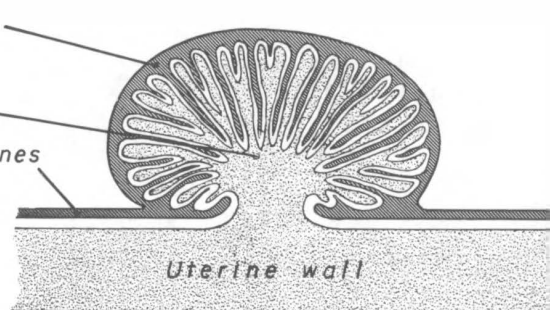


Figure 18. Placentome of the cow.



Figure 19. Normal placenta of a cow. Weight, 12 lbs., passed 4 hours after birth of calf, 52 cotyledons in gravid horn and 50 in non-gravid horn. Note those in nongravid horn are smaller.

is used at the present time only as an approximate anatomical basis for the study of placental morphology or structure³⁴ (See Figure 22).

The epitheliochorial type of placenta is found in the mare, sow, cow, and ewe. In this type six structures of varying thickness: the endothelium, connective tissue, epithelium of the endometrium and the trophoblast or chorion, mesenchyme and endothelium of the fetal tissue separate the maternal and fetal blood.

The syndesmochorial type was formerly considered present in ruminants. In this type all the tissues of the preceding type are present with the exception of the maternal epithelium. The loss of uterine epithelium was previously considered to occur in the placentomes in this type by phagocytosis and cytolysis by the cells of the trophoblast.^{1,2,40,41} Syndesmochorial relationships are found

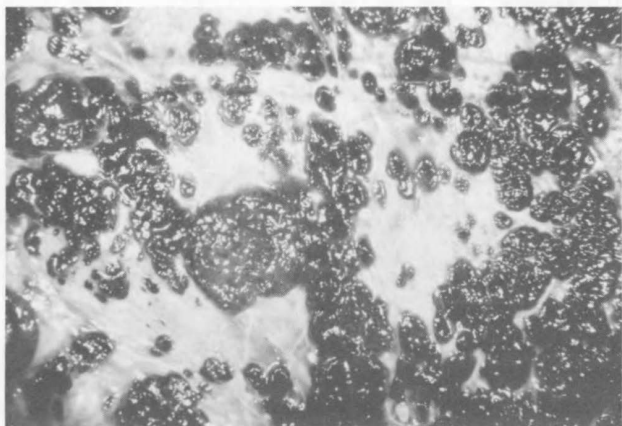


Figure 20. Adventitious placentae in a cow. (Courtesy of K. McEntee)

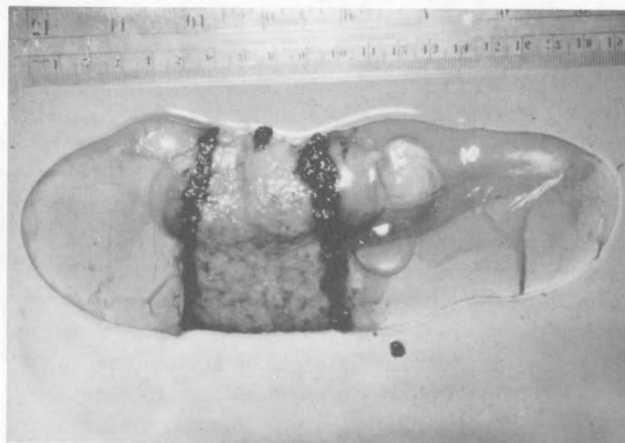


Figure 21. Zonary canine placenta.

in ruminant placentae when infections or other pathological disturbances have destroyed the maternal epithelium. At present it might be desirable to drop the term syndesmochorial, because of the great structural and functional similarity of the placentae between the mare, sow, cow and ewe.^{10-14,57}

The endotheliochorial type in the bitch and queen has the endothelium of the uterine vessels and the chorion, mesenchyme, and endothelium of the fetal tissues or 4 structures separating the maternal and fetal blood.

The hemochorial type present in primates and rodents has only the fetal tissues of the chorion, mesenchyme, and endothelium that lie or bathe in a "lake" of maternal blood since all maternal tissues have been eliminated. There is considerable difference in the structure of the hemochorial placenta in the different species.¹⁰⁻¹⁴

It was previously believed that the thickness of the placental membranes determined the efficiency of the barrier.³⁴ But the various cell layers in the placentae of the various domestic animals are not so regularly arranged. For example, in the epitheliochorial placenta capillaries migrate into intra-epithelial locations so fetal and maternal blood streams may at certain points be quite closely apposed.^{1,2} In the placenta there probably are definite transport mechanisms for most substances rather than a passive diffusion type of transport. Furthermore the inference that the epitheliochorial placenta is less efficient or more primitive than the endotheliochorial or hemochorial is not supported by the growth rates of fetuses in the various species and the type of placentalation found in both primitive and advanced species.^{1,2,10-14,63}

A third more general classification is made of the placental types of domestic animals into the **deciduate** or **conjoined**, and **indeciduate** or **apposed**. The deciduate

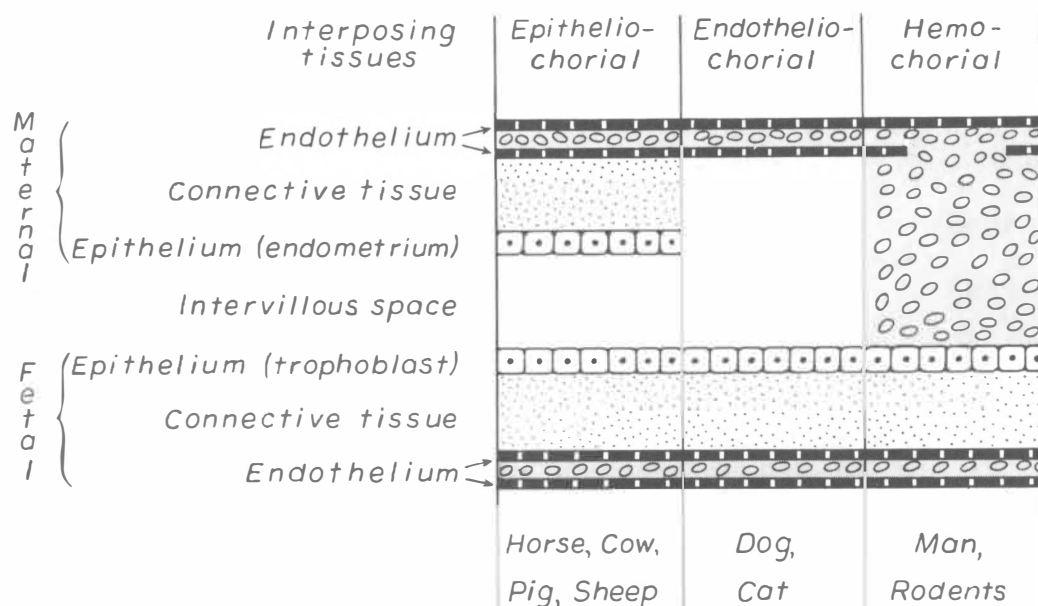


Figure 22. Diagrammatic modification of Grosser's classification of the placentae of domestic animals. (after Bjorkman)

type, or placenta vera, is that seen in primates and rodents and in a slightly modified form in the bitch and queen. In this type, the decidua composed of portions of the maternal epithelium or endothelium, submucosa, decidual cells and the fetal placenta are shed at parturition leaving a portion of the endometrium denuded. The **indeciduate** or **adeciduate** type of placenta is seen in larger domestic animals such as sows, mares, and also ruminants.¹⁰⁻¹⁴ In this type the fetal membranes and placenta are expelled at the time of parturition, leaving the endometrium intact except in ruminants in which only the surfaces of the caruncles are devoid of epithelium after the caruncle sloughs about 6 to 10 days following parturition.

The placenta is not only an organ for exchange. It can synthesize substances required by the fetus, produce enzymes necessary for the attachment of the trophoblast and intracellular digestion, and produce the hormones, estrogen and progesterone, to maintain pregnancy. It can store and catabolize other compounds. Because of the varied functions of the placenta it has some of the biochemical and even structural resemblances to adult organs such as liver, lung, kidney, small intestine and endocrine glands.

The **passive transfer of immunity** is necessary for the protection and survival of the newborn. To provide young mammals with a passive immunity against disease for a considerable time after birth, antibodies are transferred from the dam **in utero** or by the colostrum or first

milk after birth or both. The cow, ewe, doe, sow, and mare, transfer this immunity only by the colostrum.^{16,17} The human, guinea pig, and rabbit transfer immune bodies to the fetus only in the uterus through the placenta, or in the case of the rabbit through the yolk sac early in gestation by absorption from the uterine secretion. Bitches, queens and rodents pass small amounts of antibody through the placenta but the major portion comes from the early mammary secretion. In the newborn of domestic animals the intestine can absorb antibodies for only approximately 24 to 36 hours after birth. The concentration of antibody in the colostrum and the serum of the 3 to 7 day-old neonate equals and often exceeds that in the dam's serum.

Most fetuses may develop an active immunity if stimulated by certain antigens during gestation.^{44,56} The fetus doesn't develop immunologic competence simultaneously with respect to all antigens. This period may extend from early gestation to sometime after birth depending upon the antigen. This is a further defense mechanism for the fetus or newborn. Antibodies in the pregnant dam may be a factor in maintaining asepsis of the uterus to protect the fetus and placenta from infectious organisms. This study of the transfer of immunity is of great importance in treating hemolytic diseases of the newborn.

As is obvious in this discussion of placental types and the means of placental transfer of immunity, the number of layers of tissue between the maternal blood and fetal

blood have no relation to the manner in which the passive immunity is accomplished.^{16,17}

The procedures used in the examination of the placenta of the cow and mare are described because of the importance of this examination in valuable animals in providing an accurate picture of the health of the endometrium of the uterus at the time of parturition. The placenta should be examined as soon as possible after expulsion. If it is retained an excessively long period it will not be suitable for examination because of autolytic and putrefactive changes. If it cannot be examined at once it should be refrigerated. If possible the quantity, color, and nature of the fetal fluids should be noted. The membranes should be spread out to see if they are complete. Occasionally in the mare or cow the tip or apex or other portion of the fetal placenta may be torn off and left within the uterus where it may act as a focus of infection. In the mare the apices or tips of the placental horns are often edematous and if this edematous tip is incarcerated by the contraction of the uterine horn just proximal to the apex, tearing or retention of the placenta may occur.⁵⁰ The external surface of the placenta is examined for the presence of abnormal exudate or blood. The blood may be old, dark, clotted, dried, or fesh. It may rarely be in the form of dry, amber-colored, inspissated granules, called "uterine sand." Edema or necrotic leathery areas and rarely calcified portions of the allantois chorion should be noted as to their severity or extent. With the aid of a stream of water, dirt or loose material may be removed from the uterine surface of the allantois chorion and the size, nature, and uniformity of the cotyledonary villi may be observed. Evidence of clumping of villi, bare areas, necrosis, or calcification of villi are noted. Normal cotyledonary villi are uniform, smooth, and velvety. After incising the bovine allantois chorion between the dorsal and ventral rows of cotyledons and spreading it flat, the uniformity of the size of cotyledons may be checked. The presence of giant cotyledons, 15 cm. in diameter, usually indicates a lack of placentomes or a lack of placental areas or caruncles for attachment. The number in each horn is counted. There should be a total of between 75 and 120 cotyledons. Cotyledons are smaller in size in the horn opposite to the one that contains the fetus. The presence, location, number, and extent of adventitious placentae in the cow is noted. The size of the necrotic tips in the bovine placenta is observed.

Rectal examinations and slaughter-house examinations of uteri of dairy cattle from the third to eighth month of gestation frequently reveal the horn not containing the fetus to be much smaller than is normal. On examination of the uteri, fetal membranes, and placenta, there is found

a slight to complete lack of development of fetal membranes and placentae in this horn, often with a varying amount of necrosis of the membranes. The horn containing the fetus, the placenta, and the fetal membranes will appear normal. No studies have been made in the cow to determine the cause for this rather common failure for normal development of the placenta in the horn opposite to the one containing the fetus.

Evidence of thrombosis or disease of placental blood vessels is rarely observed. In placentae expelled after twin births in cattle the blood vessels should be examined for evidence of anastomosis. The amnion should be examined for evidence of disease and edema.

The fetal membranes should be weighed. In Thoroughbred mares the normal healthy placenta weighs about 10 to 14 lbs.³⁷ Mares having fetal membranes weighing more than 14 lbs. may have evidence of uterine and placental disease. The fetal membranes of cows should weigh between 6 and 18 lbs.^{1,59} with an average of 7 to 12 lbs. The weight of the foal and calf is about 6 to 10 percent of the postpartum weight of the dam. The weight of the afterbirth, or fetal membranes, is about 11 percent of the foal's weight and about 14 percent of the calf's weight. The total weight of the newborn young in the ewe and sow is about 5 to 10 percent of the dam's postpartum weight.

Tumors or anomalies of the placenta are very rare in animals. Cystic or hydatid, villous, and fibrous moles, tumorous placental growths or hyperplastic tissues and several other types that resembled hemangiomas or sarcomas have been reported in the placentae of animals.^{7,28,51} In animals they are usually benign and are shed with the fetal membranes after parturition. In dogs the hydatiform mole of the placenta was not a true tumor. The condition was due to cystic changes in the villi.⁹ They were very rare. Chorioepithelioma is rare and malignant and usually occurs after parturition from cells remaining in the endometrium.⁹

The umbilical cord connects the fetus and the placenta. In uniparous animals it is directed from the fetus toward the lesser curvature of the uterus and toward the uterine artery. In dogs and cats the umbilical stalk is attached to the zonary placenta on the opposite side of the uterus from the mesometrial attachment.^{25,26} It is composed of the allantoic and amniotic portions. The umbilical cord in the equine fetus is strong and averaged 45 to 60 cm in length, although the cord may occasionally be as long as 90 cm.^{1,62} The umbilical cord of the bovine fetus is 30 to 40 cm. in length. In the porcine fetus the cord is relatively long, about 25 cm.⁶ In the bitch and queen it is quite strong and short with a length of only 8 to 12 cm. In the cow, ewe, and usually sow, the cord

is ruptured as the fetus passes through the birth canal. In the bitch, queen, and mare the cord usually ruptures by the actions of the dam or the fetus after birth. In domestic animals it is safer from the standpoint of possible hemorrhage or infection to allow the cord to break naturally by traction than to ligate and cut it. The point of rupture in the foal and calf is about 2.5 to 5 cm. from the umbilicus at a constriction of the cord between the cord proper and the umbilical base or cutaneous navel. After rupture, the arteries retract into the body, the vein collapses, and the urachus shrinks and ceases to function. Possibly, due to the long umbilical cord and the fact that the fetus and amnion float free in the allantoic cavity, the umbilical cord in the mare is usually twisted spirally left to right or clockwise. Twisting of the cord in the mare may occasionally be severe and result in torsion and strangulation of the umbilical vessels, followed by the death of the fetus due to obstruction of the blood supply from the placenta.⁶² The umbilical cords of the other domestic animals are seldom twisted. Occasionally during pregnancy the umbilical cord may become looped around the head, neck, body, or limbs of the fetus and cause fetal death by the limitation of the blood supply.

During the early stages of development the intestines of the fetus rest partly in the umbilical cord because of their early rapid growth. Later the body walls enclose this area and the umbilical ring contracts, forcing the intestines back into the abdominal cavity. If this does not occur, an umbilical hernia results. A cross section of the umbilical cord in the amniotic portion reveals the amnion as the investing membrane. Fine granular villous elevations of the amnion occur over the umbilical cord in cows and to a lesser degree in mares, ewes, and does. Inside the investing amnion are two umbilical arteries and two umbilical veins. The latter fuse in the amniotic portion of the cord near the fetus to form a single vein. The urachus, the vestige of the yolk sac which can be seen only on histologic section, and Wharton's jelly which surrounds the above structures are also present within the amniotic membrane. The allantoic portion of the cord consists of a mass of branching vessels. The urachus expands just beyond the amniotic portion of the cord to open into the allantoic cavity.

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Teratology

Teratology is the division of embryology and pathology dealing with the abnormal development and malformations of the antenatal individual. It has also been defined as the science concerned with the causes, mechanisms and signs of structural or functional developmental deviations.³⁸⁵ Teratologic, abnormal development or arrests in development of the embryo or fetus may result in death or malformations of the antenatal or postnatal individual. In recent years rapid developments and "breakthroughs" have occurred in the fields of genetics, embryology, pathology, virology and biochemistry resulting in the new and rapidly expanding fields of molecular and cellular biology and cytogenetics.

Teratogenic agents from the environment such as radiation; chemicals; infections, especially viruses; nutritional imbalances; temperature extremes; hypoxia and endocrine or metabolic imbalances can act on germ cells, embryos or fetuses in a variety of ways to cause mutations of chromosomes or nucleic acid integrity or function, altered metabolism or enzyme inhibition and other pathogenic influences to cause either death, anomalous development, growth retardation or a functional deficit of the zygote, embryo, fetus or postnatal animal.^{33,386}

Cytogenetics is the branch of genetics devoted to the study of the cellular constituents, chromosomes and genes, which are concerned in heredity. Since a new mammalian zygote originates by the combining of an ovum and a spermatozoa to form a single cell, all of the genetic information needed to form a new enormously complex animal is present in that cell. As stated by a recent popular press article, all these instructions, if written out in English, would require several 24 volume sets of encyclopedias. Yet they are packaged into two ten-trillionths of an ounce of DNA in the nucleus of the single-celled zygote!

Molecules of DNA, deoxyribonucleic acid, a nucleoprotein which are composed of nucleotides containing

four bases, adenine, guanine, thymine and cytosine in an enormous variety of sequences arranged in ladder-like, double rows in a coiled, spiral helix, form genes which direct and control the chemical processes of each cell along certain lines by means of messenger and transfer RNA, ribonucleic acid, another nucleoprotein. These complex protein units of DNA or genes are carried on structures called chromosomes. These are best seen in anaphase, or that stage of cell division in which the chromosomes have separated and are diverging toward opposite poles of the cell. About 100,000 loci or gene locations are present on each chromosome except the Y chromosome which has fewer. The usual procedure followed in the study of chromosomes is to culture leucocytes, skin, tissue of other organs, or cells from the amnion obtained by amniocentesis for a few days so mitoses develop and then add colchicine to arrest mitosis. After a few hours hypotonic salt solution is added to the cells to swell them. They are then prepared, fixed, stained and examined under a microscope.^{89c} Chromosomes consist of a pair of chromatids held together by a centromere the location of which together with the size of the chromosome aids in the identification of the chromosomes. Their systematized arrangement in pairs and groups is called a karyotype or idiogram. The latter is a diagrammatic or formalized karyotype. Each normal cell contains two sex chromosomes and the rest of the chromosomes are called autosomes. A metacentric chromosome is one with a median centromere (X). A submetacentric chromosome is one nearly the same as the former with a submedian centromere. A telocentric chromosome is one with a subterminal centromere. An acrocentric chromosome is one nearly the same as the former with a terminal centromere (Λ). Chromosome analyses in mammals have been used to provide increased understanding of possible species differences and their evolutionary relationships. Since chromosomes can now be examined and studied, cytogenetics is providing further insights into chromosomal or genetic aberrations

Table 5. The Diploid Chromosome Number of Domestic Animals*

Species	Chromosome Number	Chromosome Characteristics
Cattle	60	58 acrocentrics, 2 submetacentric sex chromosomes
Horse	64	38 acrocentrics, 26 metacentrics
Donkey	62	
Pig	38	12 acrocentrics, 26 metacentrics
Sheep	54	47 acrocentrics, 7 metacentrics
Dog	78	76 acrocentrics, 2 metacentric sex chromosomes
Cat	38	5 acrocentrics, 33 metacentrics
Man	46	11 acrocentrics, 35 metacentrics
Goat	60	59 acrocentrics, 1 metacentric y chromosome

*Hsu and Benirschke.

as they are related to teratologic defects. (See Table 5.)

The genetic make-up of cells may be altered at the time of meiosis in a number of ways. The normal process of segregation of chromosomes may fail to occur producing **nondisjunction** resulting in an extra chromosome, trisomy or polyploidy, or a lack of a chromosome, monosomy, in the new zygote. Excellent examples of nondisjunction with an extra chromosome is mongolism or Down's syndrome in humans characterized by trisomy of chromosome 21 resulting in a total of 47 chromosomes in the individual and Turner's syndrome due to a missing Y chromosome, monosomy, of the sex chromosomes resulting in a total of 45 chromosomes. Parts of two nonhomologous chromosomes of a germ cell at meiosis may break off and be relocated on other chromosomes resulting in **translocation**. Widespread distribution in cattle of the 1/29 Robertsonian translocation and its effect on reducing fertility by increased embryonic mortality in both male and female heterozygotes has been reported.¹³⁶ When a portion of a chromosome breaks off and is lost **deletion** results. All of these abnormal processes affecting one or more chromosomes during division may also occur during mitosis in an early zygote leading to abnormalities in certain tissues or organs but not in others. Other accidents of fertilization may produce **point mutations**, **replications**, and **invasions**. It is of interest to note that cells in a variety of tumors including bovine lymphocytomas and canine transmissible tumors have irregular numbers and abnormal appearing chromosomes.²⁵⁸

The occurrence in an individual of two or more cell populations or tissues each with a different chromosome complement derived from a single zygote is called **mosaicism**. If a similar condition is present but the cell populations arise from different zygotes, as in twins with placental anastomoses, the condition is called **chimerism**.

If nondisjunction, translocation, or deletion of chromosomes is moderate to severe the zygote usually succumbs early in gestation during the period of the early embryo. Some survive longer as fetal monsters, parasites on the placenta of the normal twin, or defective individuals. Defects of the sex chromosomes, since they usually do not have much influence on organ and body development, are frequently found.

Most of the genetic defects of animals are related to one or several genes on a chromosome and at our present state of knowledge these can seldom be identified and studied, and are only determined by careful extensive breeding trials.

The mode of inheritance of genetic causes for a disease or abnormality varies greatly. It is usually due to a

natural mutation that is recessive in character but may be dominant. In diseases inherited as autosomal recessive defects neither the sire nor dam is usually affected but the disease comes from both. Dominant genes causing disease would cause defects in half of the offspring of a defective parent. Dominant defective characters are uncommon in animals. Dominance may also be incomplete. The effect of certain genes may be influenced by modifiers or other modifying genes or by incomplete penetrance of the character as in hypoplasia of the gonads in Swedish Highland cattle due to a recessive autosomal gene with incomplete penetrance. In this condition only 50 percent of the homozygous cattle are able to be clinically diagnosed. Individuals affected with a single gene defect may exhibit a great difference in the expressivity or degree to which it is manifested. Certain genes exhibit multiple or pleiotropic effects probably due to some abnormality of cellular physiology. If penetrance is fairly high, dominant factors are largely self-limiting. If there are no desirable pleiotropic effects in heterozygotes, the frequency of simple recessive factors can be kept low if a constant survey of the population is implemented.^{105,163,164,213}

The female (X) sex chromosome carries genes other than those that determine sex. While the male (Y) sex chromosome carries few genes other than those that determine sex. So genes on the X chromosome produce characteristics that are **sex-linked** such as canine hemophilia A. Recessive sex-linked defects are uncommon in animals. Characteristics found only in one sex such as cryptorchidism, milk or egg production, and "white heifer" disease are **sex-limited** in character. Certain quantitative characters such as body size, milk and butterfat production and fertility are caused by many genes, **polygenes**, or multiple factors. There is a close relationship between environmental factors and certain genetic factors as they influence the expression of disease. For example, skin lesions in hematuria in a cow with white skin will not be observed if the cow is kept from direct sunlight. Mutant defective or lethal genes are carried by nearly every animal but the heterozygosity of the animal populations usually prevent their expression except under unusual circumstances of inbreeding, selection, or accident.

The Inherited or Genetic Anomalies, Malformations or Altered States in Domestic Animals

These have been reported upon and reviewed by many authors.^{100,105,126,163,164,167,172,210,213,251,279,318,360} Some have been accurately and correctly defined as inherited con-

ditions by careful research while others have been so classified by circumstantial or limited evidence. It is unfortunate that research on inherited diseases is very costly and time-consuming. As has been noted previously, chemicals, plant poisonings, radiation, nutritive imbalances, infections and physical influences may produce identical or similar teratogenic defects as those resulting from genetic causes. In fact they may have produced the original mutations that are perpetuated in the affected chromosomes or genes.^{211b,386}

Bovine Teratology

Congenital defects affect from 0.25 to 3.0 percent of calves. About one-half of the abnormal fetuses are expelled dead or die shortly after birth.^{211a,b} In nearly all cases the defects are visible on examination. Most of the anomalies or defects involve skeletal, muscular and central nervous systems.²¹⁰ In a study of about 5000 calves sired artificially, it was reported that a high figure of 6.26 percent were abnormal at birth but of these nearly half were expelled dead at term but appeared normal. The remaining calves had a variety of abnormalities. Of 1276 calves sired by 9 bulls 7.7 percent were abnormal with a range of 3.8 to 15.7 percent.² Of 8627 calves sired by 532 bulls the incidence of congenital abnormalities was 5.49 percent with 1.77 percent being small, weak newborn, 1.05 percent having defects of bone, joints or cartilage, 2.66 percent "stillbirths," 0.16 percent nerve and eye defects, and 0.19 percent epithelial and genital abnormalities. The two greatest periods of death losses were during the first trimester of pregnancy and at the time of parturition.¹²⁶ Losses due to inherited lethals might be as high as 5 to 6 percent and in certain herds might be higher.²

Selected, common, possibly inherited, lethal and semilethal characters in cattle are:

Achondroplasia, or dwarf, "comprest" or "bulldog" calves. These are seen in all breeds but most commonly in the Hereford, Ayrshire, Angus, Charolais, Simmental and Dexter breeds. The most common type is the brachycephalic "snorter" dwarf in Herefords with a short, broad head, bulging forehead, malocclusion of the jaw, prognathism of the mandible, pot-belly, low viability and great susceptibility to bloat and dystocia. This type was generally considered to be due to a simple autosomal recessive defect with some modifiers.^{40,163,231} (See Figure 23.) The use of the profilometer in evaluation of the head shape or radiography have not proven to be highly satisfactory in the detection of carrier ani-

mals.^{83,133,183} Extensive studies on brachycephalic, dolichocephalic or long-headed, intermediate, Dexter-type, and compressed dwarfs indicated that achondroplasia was inherited in a complex manner both in a dominant and recessive form, mainly the latter, and with modifiers. The "compressed" Hereford is the result of incomplete dominance. In recent years the Hereford breed has made significant progress in reducing the incidence of this abnormality. A proportionate dwarfism in Jersey cattle,²⁴⁴ not recognizable until one year of age, has been reported. "Midget" Brahmans and "stumpy" Shorthorns caused by recessive genes as well as small guinea cattle in crossbreeds native to Florida^{199,200} have been described in which the causative gene may be dominant or incompletely dominant.¹⁰⁵ In Ayrshire, Dexter and other cattle, extreme "bulldog" calves are usually aborted about the fifth to eighth month of gestation. (See Figure 31.) Hydramnios occurs in pregnant Dexter cattle carrying a "bulldog" calf. Normal Dexter cattle are heterozygotes.

Epitheliogenesis imperfecta is a condition where skin fails to form. It occurs most commonly on the legs below the knees and hocks and on the muzzle, ears, tongue and mucous membranes. It has been described in Holsteins, Ayrshires, Jerseys, Brown Swiss, Angus and Shorthorns. It is probably a single autosomal recessive defect.^{171a,b}

Hypotrichosis congenita or alopecia is a simple autosomal recessive defect characterized by degrees of hairlessness in Holsteins,^{40,152,171b} Herefords,²²³ Durhams, Swedish Friesian cattle²⁵⁷ and Jerseys having other defects such as a short lower jaw, short ears and anophthalmia.³⁸⁹ Streaked hairlessness was reported as a sex-linked lethal in Holsteins.⁹⁶ Six types of hypotrichosis in cattle, including Guernseys, have been reviewed.^{162,165,171b} (See Figure 32.)

Ehlers-Danlos Syndrome (skin fragility), several breeds, probably hereditary.^{171b}

Ichthyosis congenita is characterized by a lack of hair and a thick scaly, horny epidermis with raw fissured skin around the body orifices. It is due to single autosomal recessive genes in Brown Swiss and Red Polled cattle.^{223,171b}

Osteopetrosis in Angus cattle may be genetic in nature. It is characterized by inferior brachygnathism, narrow nose, small size, death occurring during or shortly after a premature parturition associated with moderate hydrops amnii. The long bones, which are solid without a marrow cavity, break easily.^{130,305,257} A similar condition has been reported in Hereford calves with cystic frontal bones resembling hydrocephalus and in Simmental calves.²⁴⁹

Osteogenesis imperfecta with bone fragility, marked

joint laxity, and thin dentin (pink tooth), in Holstein-Friesian cattle in Australia (and probably Texas), due to an autosomal dominant gene.^{76b}

Acroteriasis congenita or amelia and hemimelia is seen in Holsteins, Brown Swiss and other breeds.^{105,347}

This condition is characterized by missing, shortened, deformed, or "amputated" limbs.

Ankylosis, hydrops, death and mummification of the fetus in the last month of gestation was reported in Red Danish cattle due to a pair of single autosomal recessive genes.^{347,355}

Progressive ataxia, weaver condition—in young Charolais and Brown Swiss^{211b} cattle, probably hereditary.^{284b}

Cerebellar hypoplasia and degeneration is seen in Herefords, Guernseys, Limousins and Holsteins and may be autosomal recessive in nature.^{40,167,347}

Cerebellar abiotrophy in Holstein calves, which were normal at birth, but develop ataxia, opisthotonus, head tremor, nystagmus and inability to rise due to cerebellar degeneration or atrophy at 3 to 9 months of age may possibly have an hereditary basis.³⁷⁸

Ataxia with leucodysplasia seen in Angus, Shorthorns, Jerseys, Herefords, Charolais and possibly in Holsteins and Haryana cattle at 2 or more weeks of age may be due to a number of recessive conditions.^{167,397}

Mannosidosis is lysosomal storage disease of Angus and Murray Grey calves due to a single autosomal recessive trait. It is characterized by death of a few affected calves soon after birth but more commonly the development of a progressive incoordination, ataxia, head tremor, aggressiveness and death the first year of life. Heterozygotes can be detected by the level of a-mannosidase enzyme in the blood.²²⁶

Paralyzed hind quarters have been reported in Red Danish calves at birth due to a pair of autosomal recessive genes.¹⁶⁷ A similar condition has been seen in Norwegian Red Poll cattle that also developed a keratitis.³⁴⁷

Limber legs is apparently inherited as a simple recessive trait in Jersey cattle in which the newborn, both female and male, often die at or soon after birth and if viable are unable to stand due to atonic muscles and joints that can readily be rotated, flexed or extended in any direction.^{206,207}

Curved limbs with both rear and forelimbs curved cranially, have been observed in Guernseys as an autosomal recessive trait. Calves were usually stillborn or died promptly.¹¹²

Muscle contractures and ankyloses, or arthrogryposis has been reported as a recessive defect in Dole cattle in Norway;²⁵³ and an autosomal recessive with incomplete penetrance in Charolais, associated with a cleft

palate, in England.¹⁷⁶ It has also been described in Shorthorns in Canada,⁷⁰ in Holsteins,⁴⁰ in Herefords³³⁸ and in other cattle.¹⁰⁵ Arthrogryptic defects can be due to ingestion of certain chemicals and plants and due to viral infections such as blue tongue and akabane viruses affecting the embryo or young fetus.^{131,210,211b}

Hydrocephalus in Herefords, Ayrshires, Holsteins, Shorthorns and other breeds have been reported.^{18,144,200,211b,351} It is characterized by the birth of "dummy" or "bawler" calves that are unable to nurse properly and die in several days. The heads may be enlarged or normal in size but section of the head and brain reveals distended ventricles. The disease may be associated occasionally with hydramnios, dwarfism, ocular anomalies and high copper levels in the liver.²⁶⁰ This may be due to a simple autosomal recessive gene. In Shorthorns it may be dominant with incomplete penetrance.¹²⁹

Congenital dropsy due an autosomal recessive gene has occurred in Ayrshires and Swedish Lowland cattle.^{87,147} It may be characterized by the abortion of a "bulldog" anasarctous fetus often with cysts on the tip of the ears or the birth of calves with severe persistent edema of the limbs or head. (See Figures 27 and 28.)

Rectal vaginal constriction (RVC) (anovestibular stenosis) is inherited as a simple autosomal recessive defect affecting the rectal sphincter of males and the rectal and vulvar sphincter of female Jersey cattle. This results in a firm, fibrous, unyielding stricture so that normal manual rectal examination is impossible in both sexes. In females severe dystocia, requiring an extensive episiotomy or caesarean operation, occurs at calving due to the very small vestibule.^{155,225a,b,238b}

Tibial hemimelia in Galloway calves is a single autosomal recessive defect with variable expressivity, usually bilateral agenesis, with pleiotrophic effects on the



Figure 23. Yearling brachycephalic ("snorter") Hereford dwarfs.



Figure 24. Spastic syndrome, "stretches," in a grade 9-year-old Holstein cow.

central nervous, reproductive and skeletal-muscular systems.²⁶²

Arnold-Chiari malformation is a rare congenital defect in cattle, often associated with hydrocephalus and spina bifida, that is characterized by caudal herniation of cerebellar tissue through the foramen magnum into the anterodorsal spinal canal.⁵²

Brachygnathism or underdevelopment of the mandible has been reported in nearly all breeds of cattle including Shorthorns, Jerseys and Herefords. Inheritance is more than just a simple recessive but it is not complex.^{128,341}

Microphthalmia in Guernsey, Hereford and White Shorthorn cattle along with other defects have been reported.²⁹⁸

Cleft lip and palate have been reported in Jerseys,



Figure 25. Syndactyly of the forelimbs of a Holstein calf.

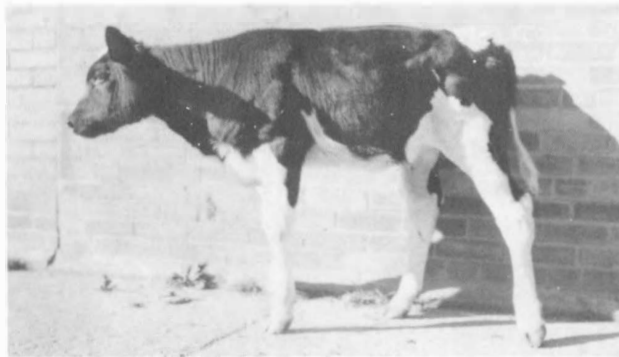


Figure 26. Spastic paresis in a Holstein calf, note the rigidly extended left hind leg.

Shorthorns and other breeds as a possible genetic defect.^{338,377}

Atresia of the anus, colon and ileum were reported as possible genetic defects in Swedish Highland cattle, Holsteins, and other breeds.^{126,256,269} However atresia ani might be related to palpation of the amniotic vesicles between 30 and 40 days of gestation.^{211b,379}

Anencephaly, cerebral hernia or "catlin mark" is an opening in the frontal and parietal bones associated with severe central nervous system defects in beef calves.⁵³ Prolonged gestation, a large fetus and dystocia in Holsteins may occur due to a fetal pituitary deficiency. (See Figures 29 and 30.)

Cardiac defects of patent ductus arteriosus, persistent foramen ovale and septal defects have been described in Herefords and Jerseys and are possibly due to genetic causes.^{213,353}

Chediak-Higashi Syndrome is an autosomal recessive

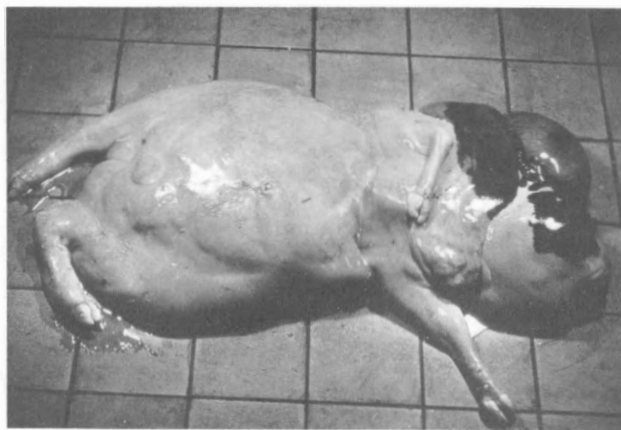


Figure 27. Congenital dropsy and anasarca in an aborted Ayrshire fetus. (Courtesy K. McEntee)



Figure 28. Congenital dropsy or edema in an Ayrshire calf. (Courtesy M. G. Fincher)

sive defect characterized in Hereford and other breeds of cattle and cats by oculocutaneous albinism (white animals or those with a ghost pattern in normally pigmented areas and hypopigmentation of the iris with photophobia), increased susceptibility to infections, tendency for prolonged bleeding, and reduced viability.^{55,211b,272,285a}

Partial alopecia, failure of horn growth, slobbering and stiffness ("Baldy calves") developing at about two months of age in calves and terminating in death by 6 to 12 months has been described in Holsteins. The evidence indicated that it was probably an hereditary condition.⁴⁰

Other inherited but generally nonlethal defects of cattle include:^{105,126,163,197,210,213,393,397}

Polydactylism in Holsteins and Herefords,^{210,303} is possibly an autosomal dominant character with incomplete penetrance.

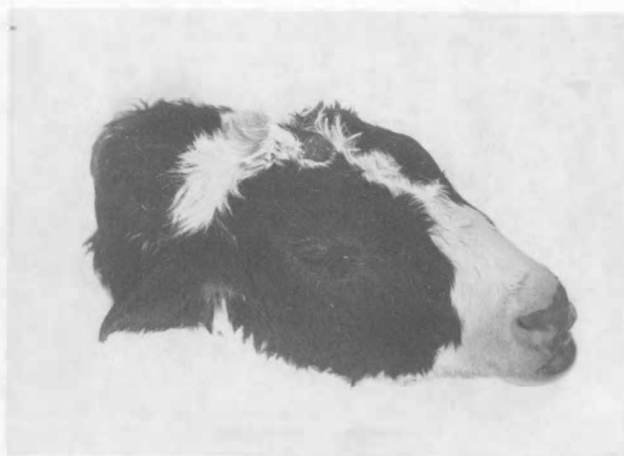


Figure 29. Cerebral hernia with a pituitary defect in an overtime Holstein fetus.

Syndactylism or "mule-foot" affecting one or both front feet or all four feet has been reported in Jersey, Holstein, Angus, Hereford, Crossbred Chianina, Hariana and other cattle, and has a single autosomal recessive mode of inheritance.^{212,264} Progeny testing using syndactylous donors, superovulation, suspect bulls, embryo transfer and fetal examination shortened the time for detection of heterozygotes.¹⁷⁴ Affected Holsteins were unable to withstand stress due to high ambient temperatures and became hyperthermic.²¹⁹ The front feet of the Holstein calves were much more frequently affected with syndactyly than the rear feet. (See Figure 25.)

Muscular hypertrophy, or "double" muscling is characterized by reduced fat deposits, light bone, thin

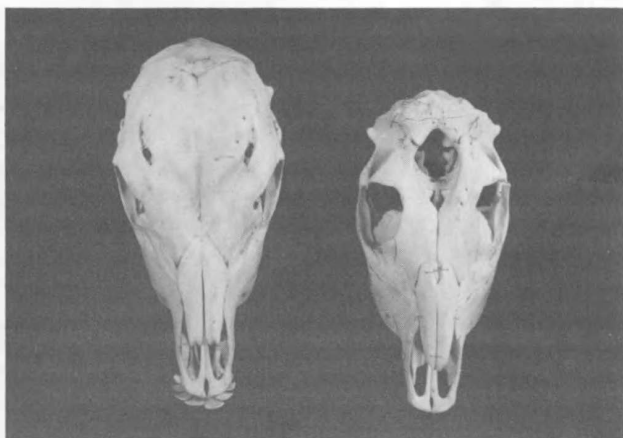


Figure 30. Skulls of a normal calf (left) and a calf with a cerebral hernia (right).

skin, and large muscles as well as severe calving difficulties, high calf mortality, and infertility. It is seen in many breeds of cattle including Hereford, Holstein, Angus, Charolais and Piedmont. It may be inherited by an autosomal monohybrid mechanism resulting in three genotypes, homozygous, heterozygous and homozygous nondouble muscled. The former can be recognized phenotypically at birth but heterozygous cattle are difficult to identify.^{233,259,265}

Umbilical hernia was described as being a probable dominant character with incomplete penetrance in Holsteins. Umbilical hernia in Holsteins may also be caused by one or more pairs of autosomal recessive genes of low frequency or by environmental factors.^{8,124,372}

Osteoarthritis and hip dysplasia in Holsteins, Angus, Galloway, Charolais, Jerseys and Herefords have been described.^{48,374} In dairy breeds the lesions were noted in the stifle joint at 5 to 13 years of age and were possibly due to a single autosomal recessive gene. In Herefords and other beef breeds the lesions were in the hip joint and it was possibly due to an incompletely penetrant dominant or recessive character.

Spastic paresis has been described in Angus, Holstein, Charolais, Shorthorn, Ayrshire, Simmental, Brown Swiss, Hereford and rarely Jersey calves usually 2 to 8 months of age with straight rear legs and a contracted gastrocnemius muscle causing the rear leg to be held off the ground and swung rigidly. It is probably due to an autosomal recessive condition with low or incomplete penetrance or even multiple recessive genes.^{76,80,191,213,304} (See Figure 26.)

Spastic syndrome, Krampfigkeit, "Stretches" may be a latent recessive condition developing at 2 to 7 years of age and characterized by spastic contractions of the



Figure 32. Hypotrichosis congenita or hairlessness in a Guernsey calf.

rear limb or limbs and back that occur intermittently in the standing animal. The condition affects Holsteins, Guernseys, Charolais, Ayrshires, and occasionally other breeds.³⁰⁴ (See Figure 24.)

Epilepsy has been reported in Swedish Red cattle, Limousin, and Brown Swiss cattle characterized by a sudden loss of consciousness preceded by a convulsion. It may be due to a recessive or dominant factor.¹⁶⁷

Lack of lid pigmentation and ocular carcinoma is seen mainly in Herefords but also Holsteins and Ayrshires exposed for long periods to sunlight. Pigmentation of the eyelid is strongly heritable so selection for pigmented eyelids can reduce the incidence of carcinomas.⁶

Ocular coloboma in Charolais cattle affecting the optic disc is common and inherited as a dominant trait but with partial penetrance in females and complete penetrance in males.¹⁰⁴

Heterochromia irides and albinism in Herefords, Charolais, Angus and Holsteins was described due to a



Figure 31. "Bulldog" achondroplastic full-term Ayrshire fetus.



Figure 33. Guernsey fetus with adenyhypophyseal hypoplasia causing a prolonged, 338 day gestation. (Courtesy of K. McEntee)



Figure 34. Epitheliogenesis imperfecta in a Yorkshire pig.

dominant mode of inheritance. These cases were more like color dilution rather than true albinism. Some affected cattle had blood dyscrasias.^{4,211b,213,217}

Congenital cataract and blindness in Jerseys and Holsteins^{50,126} may be heritable.

Strabismus and exophthalmos "cross-eyed" or "pop-eyed" in Shorthorn, Guernsey and Jersey breeds are inherited as recessive characters.^{40,126,299}

Red factor is a simple recessive defect in Holstein and Angus cattle where red substitutes for the normal black color of the hair.

Congenital porphyria, or pink tooth has been observed in Holsteins, Shorthorns and Jamaican Red cattle as a simple autosomal recessive condition resulting in photosensitivity and dermatitis of white or even pigmented skin, pink to brown teeth and bones that fluoresce with ultraviolet light. The urine may vary in color from normal to reddish-brown.^{181,255,328,373}

Protoporphyrria, due to an autosomal recessive trait is similar to porphyria and is caused by a mitochondrial enzyme deficiency of ferrochelatase. Although typical photosensitivity and dermatitis are present, the teeth, bones and urine are a normal color in the affected Limousin and crossbred cattle.^{211b,315}

Polycythemia in one- to two-month-old Jersey calves characterized by congested mucous membranes, lethargy, dyspnea and reduced growth rate was due to a single autosomal recessive gene.³⁵¹

Blood coagulation defect, Factor XI deficiency is an autosomal recessive trait of Holstein cattle causing hemorrhage after trauma with prolonged bleeding after dehorning and venipuncture.¹²²

Curly coat has been described in Ayrshires and Swedish cattle.¹⁶³

Deformed limbs or flexed pasterns has been described in Jersey cattle.^{163,210}

Wry tail is common in many breeds.^{113,150}

Wry muzzle is a common defect in Jersey cattle.^{126,163}

Screw tail (Holsteins, Jerseys, Shorthorns, Red Polled).^{126,163,213}

Vestigial tail (Holsteins, Angus, Shorthorns).^{126,213}

Taillessness (Holsteins and other breeds), possibly inherited.^{40,105}

Multiple lipomatosis (Holsteins), possibly a dominant trait with incomplete penetrance.³

Fused teats (Guernseys, Herefords).²¹⁰

Supernumerary teats (all breeds), increased incidence with inbreeding.^{27b}

Notched or short ears (Ayrshires, Jerseys).²¹⁰

"Spread" toes or splayed toes (Breed differences, due to several genes).^{236a}

Missing phalanges or "Creeper" calves (Swedish cattle).⁴⁰

"Corkscrew," "scissor" or beak claw (each due to a different recessive gene).^{236a}

Impacted premolars and "parrot-mouth" (Shorthorns).²¹³

Short spine (Norwegian cattle).^{163,213}

Ljutikow lethal.³⁴⁷

Agnathia or absence of a lower jaw (Jerseys and other breeds).²¹³

Opacity of the cornea is possibly a recessive character in Holsteins.^{40,71}

Lumpy jaw or actinomycosis and actinobacillosis is characterized by a lack of genetic resistance in Guernseys to this disease.²⁷

Ankylosis of the jaw (Norwegian cattle).^{163,213}

Dermoid cysts on cornea, (Herefords and Guernseys).¹⁴⁶

Smooth tongue (Holsteins and Brown Swiss).¹⁵⁸

Genetic diseases or conditions related to cattle reproduction and the reproductive organs such as; prolonged gestation in Holsteins and Guernseys, segmental aplasia of the mesonephric and paramesonephric ducts, imperforate hymen or white heifer disease, gonadal hypoplasia, cystic ovaries, hermaphroditism, cryptorchidism, seminal defects, failure of the median wall of the paramesonephric ducts to fuse, impotentia coeundi, penile defects, inguinal hernia, and others will be described and discussed later.^{172,173}

Equine Teratology

It has been estimated that 3 to 4 percent of foals at birth have developmental defects. Very few of the re-

ported teratologic defects in horses have been proven by adequate studies to be due to either genetic or environmental causes. This is understandable because only in recent years has considerable research been supported in horses and the cost of the animals, slow onset of sexual maturity and the long gestation period are disadvantages in undertaking genetic or long-term studies on equine malformations.^{312,360}

Some of these defects of which little is known concerning the etiology or pathogenesis include: cleft palate, angulation of limbs, microphthalmia, cardiac anomalies including ventricular septal defects and others, atresia ani, pharyngeal anomalies, hydrocephalus, persistent or pervious urachus, unilateral kidney agenesis, dentigerous cysts with fistulae, papillomatosis of the skin at birth, cataracts, "contracted," arthrogryptic foals, contracted flexor tendons, ectopic ureter and urethra, cyclopia, polydactyly, teratomas, optic nerve hypoplasia, esophageal ectasia, and others.^{159,312,349}

The inherited lethal or semilethal characters in horses are:

Atresia coli and early postnatal death in Percherons is often associated with brain defects.^{159,347}

Hemophilia or coagulation disorder is an x-linked or sex-linked recessive defect resulting in frequent bleeding episodes in Thoroughbreds and Standardbreds caused by a factor VIII (Hemophilia A) deficiency. Affected male foals have not survived to adulthood. Carrier mares have a reduced factor VIII activity.^{89,159}

Fredericksborg lethal was related to sterility in inbred white horses due to the embryonic death of about 25 percent of the embryos in early gestation.^{159,171b,347} **Iliocolonic aganglionosis** is probably a recessive, in pink-skinned, white male or female, foals of Overo spotted breeding that die soon after birth, 1 to 5 days, due to obstructive anomalies of the colon or rectum.^{156b,293,326,359}

Epitheliogenesis imperfecta affects the lower limbs and tongue and is probably an autosomal recessive defect.^{67,159,360,171b}

Hyperelastosis cutis or subcutaneous hypoplasia has been described as an inherited disease, probably recessive, in Quarter Horses. The skin is fragile and minor injury causes gaping slow-healing wounds and scarring similar to Ehlers-Danlos syndrome in humans, cattle, dogs and other animals.²²⁸

Hereditary ataxia, Oldenberg breed.^{159,347}

Wobbles or incoordination is seen in Thoroughbreds, Standardbreds, American Saddle and other breeds and grade horses. It is most common in males by a 3 to 1 ratio. It is possibly due to a recessive defect of the articulations of the cervical vertebrae causing compression of the spinal cord, usually observed in young rap-

idly growing horses. Ataxia in Shetland ponies has been reported to resemble wobbles but the condition was associated with degeneration of the spinal nerve roots. The condition might be genetic in nature.¹⁶⁷ The equine wobbler or ataxic syndrome has been described to be due to three distinct types of pathological lesions and seven other disease entities were listed that may resemble wobbles in horses.²³⁴

Cerebellar hypoplasia and ataxia is possibly a recessive genetic defect in Arabians, Gotland ponies and others.^{29,159,275}

Absence of a retina is a recessive character.⁴⁰

Combined immunodeficiency (CID) in Arabians is inherited as a simple autosomal recessive trait affecting an estimated 2.3 percent of Arabian foals with 25.7 percent of all Arabian horses considered to be carriers. Progeny testing is presently the only means of detecting carriers since no laboratory test is available. Affected foals have a lymphopenia, deficiency in T and B lymphocytes and immunoglobulin deficiencies causing them to be highly susceptible to respiratory, especially adenoviral and enteric or systemic infections that are refractory to treatment. Death usually occurs within a few weeks or months after birth.^{159,286,360}

Other immune system failures in horses include selective immunoglobulin M deficiency associated with infections and lymphoma and agammaglobulinemia. The hereditary status of these latter deficiencies is not known.^{285a,b} Deaths usually occur within 6 months to two years in these horses.

Other Possible Inherited, Generally Nonlethal Defects of Horses are:

Persistent or pervious urachus, many breeds, unknown.¹⁵⁹

Aniridia with cataracts was a dominant autosomal character in Belgians.^{101,197}

Umbilical and inguinal hernia.^{109,197}

Entropion and microphthalmia in Thoroughbreds.²¹

Brachygnathism of the mandible.^{109,197}

Subluxation of patella, ponies and others.¹⁹⁷

Ulnar and tibial malformation in Shetland ponies was caused by an autosomal recessive gene that interfered with their locomotion.¹⁴⁵

Congenital night blindness or nyctalopia has been described in Appaloosa horses. Day vision is normal but at night or at dusk affected horses bump into objects and injure themselves or are unwilling to move. A possible recessive or congenital mode of inheritance is suspected.³⁹⁰

Strabismus or hypertropia is also suspected to be an hereditary defect in Appaloosa horses. Corrective surgery may be indicated.¹¹⁹

Angular limb deformities, carpal bone hypoplasia, osteochondrosis dissecans and congenital goiter have been associated and may have an hereditary component.^{241,242}

Multiple exostosis is due to a single dominant autosomal gene in Quarter Horses^{159,247} and Thoroughbreds that affects endochondral bones during skeletal development, usually prenatally, may impair future performance.³⁴⁰

Heaves, pulmonary emphysema or chronic obstructive pulmonary disease is produced by a hypersensitivity to environmental allergens. As in humans there is a family predisposition that is probably genetic.^{197,360}

Roaring, laryngeal hemiplegia. Recent studies have confirmed the familial and hereditary status of this disease.^{57a,65,109,197,294}

Dysplasia of the hip (Dole horses).⁴⁰

Some of the above conditions and others sometimes referred to as genetic diseases such as: splints, ringbone, spavin, scrotal hernia, and others may or may not be genetic in horses as few actual breeding trials have been conducted. Severely defective animals are usually immediately destroyed.

Porcine Teratology

Inherited congenital defects are fairly common in swine with an incidence of 1.25 percent.³³⁴ Since newborn piglets are relatively immature and their economic value low many defective pigs if they cannot nurse vigorously die within several days of birth. Thus fairly minor defects may have a lethal effect. In recent years many congenital defects previously considered to be probably genetic have been shown to be due to environmental factors such as: poisonous plants, chemicals, viral infections and nutritional deficiencies affecting the porcine embryos or fetuses during the gestation period. Selected, fairly common malformations of swine due to genetic causes are listed.

The inherited lethal or semilethal characters in swine are:

Cerebral hernia, "Catlin" mark, cranioschisis, is probably an autosomal trait in Poland China pigs.^{160,347}

Hydrocephalus is reported in Duroc Jerseys due to recessive genes.^{163,347}

Paralysis of the hind limbs due to spinal cord lesions. This is a recessive, semilethal character.^{160,167,358}

Atresia ani.^{160,251,358,397}

Thickened forelimbs is a recessive often lethal defect.^{40,251,347}

Acroteriasis congenita, "amputated," is caused by a single autosomal recessive gene.^{163,347}

Cleft palate, or palatoschisis, is seen occasionally with harelip in the Large White and Poland China breeds and transmitted as a single autosomal recessive.^{160,251,254,347}

Arthrogryposis or flexed or extended rigid limbs may be caused by a single autosomal recessive gene but is also commonly caused by plants or chemicals ingested during gestation.^{97,160}

Other Inherited Generally Nonlethal Defects of Swine are:

Porcine stress syndrome (PSS) malignant hyperthermia is a genetic disease in susceptible pigs brought on by stress such as fighting, restraint, transport, hot weather, mating, forced exercise and halothane anesthesia. At slaughter carcasses of affected swine have pale, soft exudative muscles and small adrenal glands weighing less than two-thirds normal gland weight.^{194b} During stress susceptible pigs develop tachycardia, tachypnea, erythema, cyanosis, rigid muscles, increased body temperature often followed by death. It is reported most often in Poland China, Yorkshire, Landrace and Pietrain breeds.^{19,160,346,382} Selection for the heavily muscled meat type pig¹⁶³ has favored the selection of pigs susceptible to the porcine stress syndrome. It has been suggested that this syndrome is inherited by a modified single dominant gene or two dominant genes acting together. A practical test to determine susceptible or carrier pigs is not available but selective breeding has proven effective in reducing the incidence of this common condition in many herds. Dogs, horses and heavily muscled cattle have been reported to suffer a similar syndrome under stress or halothane anesthesia.

Hemophilia, porcine von Willebrand's disease is an autosomal or incompletely dominant defect with variable penetrance affecting Poland China swine. It is clinically characterized by mild to severe hematoma formation, lameness, and prolonged or fatal bleeding after surgical procedures or farrowing. Affected pigs have a deficiency of blood Factor VIII.^{85,271}

Renal cysts in Landrace pigs were reported as an autosomal dominant gene while the number of cysts was polygenic. No clinical signs were noted.³⁸¹

Epitheliogenesis imperfecta in Berkshires and Yorkshires. (See Figure 34) is a recessive lethal or sublethal defect.^{317,171b}

Wattles, or tassels.^{163,171b,347}

Screw or kinky tail is due to either a single recessive factor with modifiers or a dominant factor with low penetrance.^{86,160,347}

Umbilical hernia^{160,163}

Inguinal or scrotal hernia, sex-limited inheritance with a double recessive genotype. About 1.5 percent of males are affected.^{160,163,251}

Hypotrichosis congenita.^{160,163,171b}

Congenital bent legs.^{251,347}

Split ears, deformed rear quarters and occasionally cleft palates in Tamworths and Poland Chinas.^{160,347}

Congenital porphyria is a dominant character. No photosensitivity is evident.^{180,347}

Cryptorchidism^{40,160,347}

Syndactyly and polydactyly are probably caused by simple autosomal dominant genes.^{160,251,347}

Hermaphroditism^{160,197,288}

Inverted teats is probably a simple recessive trait.^{160,197,397}

Hypertrophy of muscle, Pietrain pig in Belgium¹⁶³

Dermatosis vegetans, is a semilethal autosomal recessive condition.^{89a,171b}

Chromosomal abnormalities causing embryonic mortality were present in up to 30 percent of porcine blastocysts.²³⁷

Microphthalmia, anophthalmia is possibly due to a dominant gene with low penetrance. It may also be due to a vitamin A deficiency.^{160,251,347}

Barker, or neonatal respiratory distress, syndrome of the Large White breed is probably an autosomal recessive defect involving lung tissues, hypothyroidism, hairlessness, retarded ossification and reduced adrenocortical activity. Affected piglets developed respiratory distress and hypothermia soon after birth and died. Gestation length of sows with affected litters was slightly longer than normal even though affected pigs had evidence of prematurity.³⁹⁴

Myoclonia congenita, congenital tremors or "shaker" pigs has been reported as caused by a monogenic sex-linked factor in Landrace pigs and an autosomal recessive gene in Saddleback pigs. It has also been reported in pigs due to hog cholera virus, pseudorabies virus and a third unidentified virus infecting swine fetuses in utero. Tremors in newborn piglets have also been reported from sows wormed with trichlorfon between 45 and 63 days of gestation. Mortality in severely affected pigs is high due to the inability to nurse and the resulting starvation.^{88,135,196,284}

Splayleg or spraddle-legs, myofibrillar hypoplasia is probably not due to genetic causes unless associated with congenital tremors. It has been reported to be caused by slippery floors, chemicals or nutritional deficiencies. This condition may be a common expression of congenital tremors.^{88,135,160,251}

Hereditary lymphosarcoma in piglets has been re-

ported as an apparently autosomal recessive trait that can be diagnosed only after one month of age. No homozygous recessive pigs have survived to maturity.²⁴³

Cerebrospinal lipodystrophy, GM2 Gangliosidosis is a storage disease characterized by poor growth rate, "goose stepping" of rear legs, and recumbency at 4 to 6 months of age. It is an autosomal recessive trait in Yorkshires.²⁸⁷

Ovine and Caprine Teratology

In sheep the incidence of congenital defects ranges from 0.2 to 2.0 percent of all lambs born. One report on over 54,000 lambs over a 15 year period revealed bilateral cryptorchidism occurred in .0005 percent, wry neck in .0007 percent and crooked legs, unilateral cryptorchidism and "undershot" or "overshot" jaws in .001 percent of the lambs. "Stillbirths" occurred in 4.4 percent of the parturitions. Inbred groups of ewes had the highest number of defects. The musculoskeletal, cardiovascular and urogenital systems are most commonly affected.^{77,79,99} Many nongenetic environmental agents as well as genetic influences are responsible for teratogenic defects in sheep. As in the other species of domestic animals nongenetic defects can mimic very closely genetic defects. Most genetic defects are recessive in character in sheep. The following are selected, fairly common genetic defects reported in sheep.

The inherited lethal or semilethal characters in sheep and goats are:

Muscle contracture, ankylosis, arthrogryposis or flexed limbs and wry neck. These are expelled dead and are due to simple recessive genes or nongenetic causes.^{296,347}

Paralysis of hind limbs is seen in Corriedales as a simple recessive.^{296,347}

Perosomus elumbis is also common in sheep and due to an unknown cause.³¹⁹

Rigid fetlocks is characterized by a deformed body, short wool and hernias and is probably caused by a recessive gene.^{296,347}

Acroteriasis congenita or amputated limbs.^{77,79,296,319,347}

Lethal gray is seen in gray Karakul lambs as an incomplete dominant character with obstruction of the gut and possibly nerve damage.^{167,296,347}

Collagen dysplasia is due to a simple autosomal recessive lethal gene and causes the skin to be very friable and easily torn.^{77,79,319}

Lethal myodystrophia,^{319,347} inheritance is questionable and may also be due to vitamin E or selenium deficiency.

Dwarfism or achondroplasia is seen in Ancon sheep due to a simple autosomal recessive gene.^{77,163,296,347}

Agnathia is observed in a variety of forms and is due to a recessive gene as well as an environmental agent.^{77,296,319,347}

Cerebellar hypoplasia, ataxia, or "daft" lambs, is a simple autosomal recessive character in Corriedales.^{77,163,147}

Caprine oligosaccharide (lysosomal) storage disease or B-mannosidosis is due to an inborn, apparently genetic, lethal defect in Nubian goats due to a deficiency in lysosomal B-D mannosidase. Heterozygotes showed a partial enzyme deficiency. Affected kids of both sexes exhibited severe neurological deficits with axonal pathology and extensive demyelination after birth.^{506,178,179}

Other Hereditary Generally Nonlethal Defects in Sheep and Goats

Malocclusion, brachygnathism or prognathism¹⁶³

Hypotrichosis congenita^{163,171b,319}

Epitheliogenesis imperfecta is uncommon but usually affects the lower limbs, tongue and palate of lambs and it is possibly of genetic origin.^{40,171b,306}

Hermaphroditism is common in polled goats, especially Saanen.³⁰⁰

Cryptorchidism is an autosomal recessive character in goats and sheep or an autosomal dominant with incomplete penetrance in sheep.^{77,79,296,319}

Yellow fat is a simple recessive character.^{77,79,163,296}

Anury ("no tail"), brachyury or polyury are commonly associated with other defects of sheep.^{77,79,163,319}

Myotonia congenita is an inherited disease of goats characterized by a sudden development of muscle rigidity and in some prostration when they are startled.^{40,42,163,167}

Entropion has probably a complex polygenic inheritance either autosomal dominant or homozygous recessive. Rams that are affected or have produced affected lambs should be eliminated.^{40,64,229,296,319}

Hyperbilirubinemia of Southdown and Corriedale sheep is a sublethal single recessive gene with full penetrance and characterized by jaundice, photosensitization, renal fibrosis and pulmonary edema at 1 to 2 months of age.^{20,239,319}

Wattles in sheep and goats are due to a single dominant gene.^{197,296}

Hydrocephalus¹⁹⁷

Atresia ani is possibly hereditary and commonly associated with other developmental defects. Three-quarters of affected lambs were male.^{78,197}

Sperm granuloma is seen secondary to anomalies of the mesonephric or efferent ducts in male goats.¹⁹⁷

Canine Teratology

With the control of most of the infectious diseases in humans, a recent great interest has developed in environmental concerns, particularly with chemical agents, radiation, and nutritional deficiencies and their effects on the embryo and fetus. Many studies are now underway that are greatly expanding our knowledge of environmental teratogens as well as the genetic teratogenic diseases. Veterinary medical genetics particularly in polytocous laboratory and small domestic animals is a rapidly and expanding discipline along with the field of environmental teratogens which can produce disease conditions closely resembling genetic defects. These latter animals, because of early maturity, short gestation periods, large numbers of embryos and fetuses, and ease of handling and low economic cost and maintenance are being extensively used as models of human diseases. Such research is also providing great and rapid advances in veterinary medicine.^{177,240,386,392}

Because of the very great number of congenital defects in which most are possible, probable or proven to be genetic in dogs and their wide dispersion in the various breeds, the author in selecting and listing the more common genetic abnormalities will rely heavily on the reviews of Hutt,¹⁶⁴ Erickson et al.¹⁰⁰ and Patterson²⁷⁹ and Barnett.^{22,23}

The inherited lethal, semilethal and nonlethal defects in dogs are:

Eye abnormalities

Cataract in many breeds, dominant or recessive.^{100,121}

Distichiasis, a double row of eyelashes, in Pekinese, Pug, Poodles and Cocker, possibly hereditary.¹⁰⁰

Collie-eye anomaly, chorioretinal dysplasia, in Collies, Shetland Sheepdogs and others mainly recessive.^{23,100,117,164}

Entropion, in many breeds, mode of inheritance unknown.^{100,279}

Ectropion, in several breeds, as Beagles, Spaniels, Saint Bernards and others, mode unknown.^{100,164}

Primary glaucomas, in Beagles, Cocker, Miniature Poodles and Bassett Hounds, recessive in Beagles.^{23,100,117b,164}

Hemeralopia in Alaskan Malamutes, recessive.^{23,100,164}

Lens luxation and secondary glaucoma, Terrier breeds,³⁸⁴ probably an autosomal recessive.

Microphthalmia, in homozygous merle dogs in merle breeds.^{100,117}

Microphthalmia with multiple colobomas in Australian Shepherds,^{119b,120} recessive with incomplete pen-

etrance, and more severe in predominantly white pups.

Central progressive retinal atrophy, Retrievers, Springer Spaniels and Border Collies, probably dominant with incomplete penetrance.^{23,100,117}

Generalized progressive retinal atrophy or rod-cone dysplasia, in many breeds, recessive.^{23,100,391}

Retinal dysplasia, Terriers, Sealyham, Labrador Retriever and English Springer Spaniels, recessive.³²⁴

Persistent pupillary membrane, Basenji, Corgi and Cocker Spaniels, probably dominant.^{116,117}

Ear abnormalities

Deafness, associated with white and merle coat colors, Dalmations, Sealyhams, English Setters, Bull Terriers, Foxhounds, Fox Terriers and breeds carrying the merle gene,^{143c} recessive in Bull Terriers, others unknown.^{100,279}

Central Nervous System Abnormalities

Scotty cramp, recurrent tetany, in Scottish Terriers,^{100,279} recessive.

Amaurotic idiocy, C.N.S. Storage Disease, GM2 gangliosidosis, German Short-Haired Pointer, probably recessive.^{100,279}

Thoracic Hemivertebra, in German Shorthair Pointer, autosomal recessive.^{203b}

Juvenile amaurotic idiocy, neuronal ceroidlipofuscinosis, in English Setters and Chihuahuas, recessive.^{100,295}

Ataxia, degeneration of spinal cord, in Fox and Jack Russell Terriers, probably recessive.^{100,279}

Cerebellar hypoplasia, and ataxia, in Airedales, Smooth-Haired Fox Terriers and Chow Chows, possibly hereditary.^{39,195}

Cerebellar degeneration and abiotrophy in Gordon Setters, Collies, Kerry Blue Terriers, autosomal recessive.^{73,74,140}

Epilepsy, convulsive seizures, in Keeshounds, German Shepherds, Beagles, Collies, and Poodles, possibly recessive.^{100,279}

Globoid leukodystrophy or Krabbe's Disease in West Highland White and Cairn Terriers, Dalmations, Blue Tick Hounds and Miniature Poodles. Recessive in the Terriers, possibly recessive in others.^{100,279}

Hydrocephalus, internal in the Cocker Spaniel, English Bulldog, Beagle, Chihuahua and other small breeds, probably recessive.^{100,279,333}

Neurotropic osteopathy, neuropathic necrosis, gnawing of digits in Pointers, probably recessive.^{100,279}

Neuromuscular disorders, myotonia, and muscular atrophy, in Labrador Retrievers, Golden Retrievers, Brittany Spaniels, Chow Chows, Swedish Lapland dogs,

Irish Terriers and others, recessive, possibly sex-linked and polygenic in some breeds.^{100,203,279}

Neuronal abiotrophy in Swedish Lapland Dogs, recessive.^{100,279,316}

Quadruplegia with amblyopia, "swimmers" in Irish Setters,^{100,279} recessive.

Neurospinal dysraphism or syringomyelia in Weimaraners and others, due to a codominant gene with reduced penetrance and variable expressivity.^{98b,100,279}

Progressive degenerative neurologic disease or myelopathy, in German Shepherds, probably genetic.⁴¹

Behavioral abnormalities including aggressiveness, and abnormal maternal behavior in several breeds especially Poodles, Cocker Spaniels and German Shepherds, probably polygenic.^{100,279}

Urinary System Abnormalities

Cystinuria, cystine stones in a number of breeds including Dachshunds and Terriers, sex-linked recessive.^{100,279}

Bilateral renal cortical hypoplasia leading to uremia and secondary hypoparathyroidism in Cocker Spaniels, Norwegian Elkhounds and others,^{100,279} probably recessive.

Excess uric acid secretion and stones in Dalmations, recessive.^{100,279}

Ureteral ectopia with urinary incontinence especially in females, in Siberian Huskies, West Highland White Terriers, Fox Terriers and Miniature and Toy Poodles.²

Blood and Lymphatic Abnormalities

Anasarca, generalized edema in English Bulldog^{100,279} and Beagle, possibly a lethal genetic defect.

Lymphedema involving the hind legs and occasionally the body in Labrador-Poodle crosses and German Shorthair Pointers.^{100,279} Severe cases are lethal and moderate cases may recover in several months after birth, dominant.

Anemia associated with chondrodysplasia in Alaskan Malamutes, associated pleomorphically with recessive dwarf gene.^{100,279}

Pyruvate kinase deficiency, hemolytic anemia, in Basenji, probably genetic.^{100,279,350}

Factor VII deficiency, prolonged bleeding, in Alaskan Malamutes and Beagles, recessive.^{100,279}

Factor VIII deficiency, hemophilia A, prolonged bleeding, in many breeds, sex-linked, recessive.^{100,279}

Factor IX deficiency, hemophilia B, prolonged bleeding in Cairn Terriers, Coonhounds, and St. Bernards, sex-linked recessive.^{100,279}

Factor X deficiency, prolonged bleeding in newborn

and young adults, in Cocker Spaniels, incomplete dominant.^{100,279}

Factor XI deficiency, prolonged bleeding in Springer Spaniels, incomplete dominant or possibly incomplete recessive.^{100,279}

Platelet disorders or defects, prolonged bleeding in Otter, Bassett and Fox Hounds, and Scottish Terriers, incomplete dominant.^{100,279}

von Willebrand's disease, low factor VIII with prolonged bleeding time in German Shepherd, Miniature Schnauzer, Scottish Terrier and others, incomplete dominant.^{85,100,279}

Blood group incompatibility (mainly A system) in all breeds, dominant.²⁷⁹

Cyclic neutropenia, gray collie syndrome, in silver gray Collies, with cycles of neutropenia and local or systemic infections, lethal autosomal recessive.^{100,279,285a}

Granulocytopathy syndrome in Irish Setters, autosomal recessive.^{285a}

Cardiac anomalies including atrial and septal defects, valvular stenosis (pulmonary), tetralogy of Fallot, dextroposition of the aorta, mitral valve defects, patent ductus arteriosus and persistent right aortic arch in many breeds, either polygenic or unknown.^{81,100,279}

Respiratory System Abnormalities

Laryngeal hypoplasia in Skye Terriers, recessive.¹⁰⁰

Collapsed trachea in Chihuahua, toy and miniature breeds, possibly genetic or unknown.¹⁰⁰

Tracheal hypoplasia in English Bulldogs,¹⁰⁰ possibly genetic and lethal.

Stenotic nares and elongated soft palate, in brachycephalic breeds, possibly genetic.¹⁰⁰

Alimentary System Abnormalities

Esophageal dilatation or achalasia with persistent vomiting and often aspiration pneumonia, in many breeds, possibly recessive or polygenic.^{63,100,279}

Glossopharyngeal, "bird-tongue" defect, lethal recessive.^{100,164,279}

Hepatitis with secondary cirrhosis and slow loss of condition, copper toxicosis in Bedlington Terriers^{175,279,364} autosomal, recessive.

Hepatic encephalopathy associated with anomalous portosystemic anastomoses (patent ductus venosus) and hepatic insufficiency, in a number of breeds, congenital and unknown.^{24,59,363}

Pancreatic degenerative atrophy, with a deficiency of pancreatic hydrolases in German Shepherds, probably an autosomal recessive or autosomal dominant with incomplete penetrance.³⁷⁶

Skin Abnormalities

Dermoid sinus, in Rhodesian Ridgebacks, possibly incomplete dominant or recessive.^{100,171b}

Hairlessness in Ceylon, Mexican, Turkish and Chinese breeds,^{100,279} dominant; homozygous dominant is lethal.

Fragility, hyperextensibility of skin or Ehlers-Danlos syndrome, in Springer Spaniels, Greyhounds, Beagles and English Setters,^{100,171b,279} dominant.

Hypotrichosis or follicular dysplasia in Miniature Poodles, Whippets and mongrels,^{56,100,171b,247a,279} unknown, possibly autosomal dominant and sex-linked or sex-limited.

Symmetrical alopecia or ectodermal dysplasia in Whippets and Miniature Poodles, unknown, possibly genetic.^{100,171b,279}

Atopic, hypersensitive dermatitis in Beagles, Poodles, Dalmatians, Highland White, Scotch and Wire-haired Fox Terriers,^{100,279} possibly genetic, unknown.

Generalized demodectic mange, in a number of breeds,¹⁰⁰ possibly an hereditary T-cell-mediated deficiency, unknown.

Nasal solar dermatitis, in Collies and Shetland Sheepdogs¹⁰⁰ with lack of skin pigment on nose, unknown.

Ichthyosis, in mongrel and Doberman Pinschers,^{171b,248} unknown.

Skin-fold pyoderma, often requires surgery to correct, in lip-folds in Cocker Spaniels and St. Bernards, folds on bridge of nose in brachycephalic breeds, and tail-folds in screw-tail dogs such as Boston Terrier, English Bulldogs, Schipperke and Pugs, probably an inherited predisposition.²⁰²

Skeletal System Abnormalities

Cranioschisis, skull fissure(s), in Cocker Spaniels,^{100,279} probably lethal recessive.

Achondroplasia of limbs in Dachshund and Basset Hounds,²⁷⁹ incomplete dominant.

Achondroplasia and pseudoachondroplastic dysplasia,^{100,302} in Miniature Poodles and Scottish Terriers, probably a recessive.

Dwarfism (achondroplasia with anemia) in Alaskan Malamutes,^{100,279} recessive.

Carpal subluxation in Irish Setter and Labrador Retrievers,^{100,279} sex-linked recessive.

Anury, tail-less or brachyury, short, kinked tail in Cocker Spaniel (both) and Beagle and English Bulldog (latter),^{100,279} probably recessive.

Cervical vertebral deformity, spondylolisthesis, in Basset Hounds, Great Danes, and Doberman Pinschers,^{100,279,361} unknown.

Cranio-mandibular osteopathy, "lion jaw" in Cairn, Scottish and West Highland White Terriers and Labrador Retrievers,^{100,279} possibly hereditary.

Predisposition to intervertebral disc disease in chondrodystrophic breeds as Beagles, Cocker Spaniel, Dachshund and Pekinese, unknown.

Multiple epiphyseal dysplasia in Beagles and Miniature Poodles,^{100,279} recessive.

Hip dysplasia in many breeds, especially German Shepherds, Great Danes, Newfoundlands, St. Bernards, Golden Retrievers, Siberian Huskies, also Cocker Spaniels and Old English Sheepdogs, polygenic. This is the most common canine congenital defect.^{100,232,279}

Polydactyly or dew claws in many breeds, especially in rear limbs, recessive in Collies, dominant in other breeds.^{100,279}

Elbow dysplasia, ununited anconeal process, in many breeds^{100,279} especially the large and giant breeds, and Cocker Spaniels,¹⁰⁰ mode of inheritance is unknown.

Premature closure of distal ulnar physis and subluxation of elbow, in Skye Terriers, recessive.²⁰⁹

Ulnar dysostosis and elbow joint abnormalities, in Basset Hounds, possibly genetic.²⁹⁷

Patellar luxation, either medial or lateral, usually the former, in many small breeds as Pomeranians, Yorkshire and Boston Terriers, Miniature and Toy Poodles and Chihuahuas,^{100,279} possibly recessive, polygenic or unknown.

Otocephaly, partial agnathia and hydrocephaly, in Beagles,^{100,279} possibly polygenic.

Odontoid process hypoplasia or dysplasia in Miniature Poodles, Pomeranians, Yorkshire Terriers, and other small breeds,^{100,279} unknown.

Osteogenesis imperfecta in Bedlington Terriers, Elkhounds and Poodles,²⁷⁹ unknown, possibly nutritional in dogs on only meat diets.

Over- and undershot jaw in Cocker Spaniels and long-haired Dachshunds,^{100,279} unknown.

Polyostotic fibrous dysplasia, cyst formation in distal metaphyses of ulna and radius in Doberman Pinschers,^{100,279} possibly genetic.

Osteochondrosis or osteochondritis dissecans, in many breeds,^{100,266} possibly genetic and environmental causes.

Multiple cartilagenous exostoses in the dog,^{100,114} a number of breeds, unknown.

Dislocation of the shoulder in small breeds, miniature Pinschers and Poodles, Chihuahuas, Pomeranians, Griffens, and Wire-haired Fox Terriers,¹⁰⁰ unknown.

Short spine in Greyhounds and Shiba-Inu (Japan),^{100,279} unknown.

Spina bifida occulta, and spinal dysraphism, in

English Bulldogs,^{100,279,387} unknown, with urinary and fecal incontinence.

Perthes disease of hip in Fox and Cairn Terriers and Alsations,²⁷⁹ unknown.

Elbow joint malformation in Afghan Hounds,¹⁰⁰ unknown.

Miscellaneous Malformations in Dogs

Cryptorchidism in most breeds,²⁷⁹ sex-limited, recessive or unknown.

Inguinal hernia in Basset Hound, Basenji, Cairn Terrier, Pekinese, West Highland White Terrier and Lhasa Apso,^{100,279} genetic basis is unknown.

Umbilical hernia in Cocker Spaniels and Bull Terriers is recessive; in Collies, Basenji, Pekingese, Pointers, Weimaraners and Airedales,^{100,279} unknown.

Neoplasia-hereditary predisposition in certain breeds such as Cocker Spaniels and Boxers.^{100,279}

Osteogenic sarcoma in giant breeds.

Mastocytoma in Boston Terriers and Boxers.

Pituitary Tumor in Boston Terriers.

Melanoma in Scottish Terriers.

Oligodendroglioma in English Bulldogs, Boston Terriers and Boxers.

Proneness to vaginal prolapse, Boxers and Bulldogs, possibly genetic.

Proneness to disease of the ear canal, excessive hair in ear canal or heavy "floppy" ears in Poodles, Bedlington, Sealyhams, Wirehaired Fox Terriers, Cocker and Springer Spaniels and others, unknown.

Feline Teratology

Cats have the lowest incidence of congenital defects of the domestic animals. The most common abnormalities are those affecting the central nervous system, especially cerebellar hypoplasia due to the feline panleukopenia virus, eyes and eyelids, feet, tails and palates. Genetic defects are uncommon and environmental causes of defects are not well known. Reviews of feline abnormalities have been reported by Saperstein et al.,³¹⁸ Foley et al.¹⁰⁹ and Colby and Stein.⁵⁴

Inherited lethal, semilethal or nonlethal defects in cats are:

Abnormalities of the central nervous system

Feline tremors,^{109,318} probably an autosomal recessive trait.

Hydrocephalus, in Siamese,^{109,318} lethal and possibly recessive, may be associated with cleft palate and hairlip.

Craniofacial malformation in Burmese kittens, characterized by an enlarged cranial cavity with skull defect, small eyes or anophthalmia, absence of nostrils and duplication of upper jaw, palate, and "whisker pads," possibly an autosomal recessive.^{74b}

Spina bifida in Manx cats, rare in other breeds,^{109,318} is a dominant with incomplete penetrance often associated with taillessness and syringomyelia.

Neuroaxonal dystrophy with progressive ataxia,^{109,318} an autosomal recessive, developing about 1 to 2 months of age, rare.

Exencephaly, meningocele and related to anencephaly,^{109,318} unknown cause, may be associated with spinal column anomalies and cleft palate.

GM, Gangliosidosis, a lysosomal storage disease, Niemann-Pick disease in Siamese cats,^{109,318,375} an autosomal recessive lethal trait with C.N.S. signs and neuronal degeneration from 2 to 4 months of age.

Globoid leukodystrophy,¹⁰⁹ progressive neuronal deterioration with death at 2 to 6 weeks of age, possibly an autosomal recessive or unknown.

Mucopolysaccharidosis, Hurler's Syndrome, lysosomal storage disease, in white domestic short-haired and Siamese cats,¹⁴³ an autosomal recessive trait, characterized by presence or absence of dwarfism, facial dysmorphism with frontal bossing, depressed nasal bridge, small ears and cloudy cornea, hip subluxation, fusion of cervical vertebrae and pectus excavatum. The urine can be tested for excess mucopolysaccharides.

Abnormalities of the Eyes

Chediak-Higashi Syndrome, in blue-smoke Persians,^{32,55,285a,291} The iris is pale yellow-green and ocular fundi are hypopigmented. Cataracts and nystagmus were present in cats with this syndrome as well as photophobia, prolonged bleeding time and increased susceptibility to infection, a simple autosomal recessive defect.

Central retinal degeneration,¹⁰⁹ most common in Siamese, possibly hereditary.

Diffuse outer segment retinal degeneration in Persians and others,^{109,376b} probably autosomal recessive.

Strabismus, common in Siamese,³¹⁸ possibly hereditary.

Microphthalmia or hypoplastic eyeball,³¹⁸ often with other eye defects, cause unknown.

Infantile glaucoma—rare condition,³¹⁸ ectopic lens may be associated with glaucoma.

Eyelid agenesis—agenesis of outer half of eyelids, in domestic shorthaired cats and Persians,³¹⁸ unknown cause.

Dermoid near limbus or on cornea,³¹⁸ seen occasionally.

Cataracts, nuclear,³¹⁸ most common type, cause unknown, possibly hereditary.

Abnormal visual pathways, in Siamese,¹⁰⁹ often related to albinism or light coat color.

Abnormalities of the Ears

Deafness, Waardenberg Syndrome,^{61,109,318} associated with white coat color and one or two blue eyes (iris), autosomal dominant gene with complete penetrance for white coat, with incomplete penetrance for deafness and blue eyes. May be associated with lowered fertility and reduced disease resistance. Atrophy and dysgenesis of the organ of Corti is the cause for deafness.

Folded ears,¹⁰⁹ associated with short tail and hobbling gait, inheritance undetermined.

Four ears,^{109,318} with extra pinna on each side of head, rare, simple autosomal recessive trait.

Abnormalities of the Musculoskeletal System

Achondroplasia or dwarfism^{109,318} is an autosomal recessive trait.

Ectrodactyly or agenesis of all or part of the digit of the forepaws^{109,318} hereditary heterozygous condition with variable expressivity.

Arrested development of the long bones of the forelimb, "kangaroo" cat,^{109,318} possibly a sex-linked inheritance.

Hip dysplasia, rare, in Siamese and Persian and other cats,^{109,318} possibly genetic.

Polydactyly,³¹⁸ extra digits, usually on forepaws, common due to autosomal dominant gene with variable expressivity.

Tail absent or no coccygeal vertebrae ("rumpy"),^{54,72,109,318} several coccygeal vertebrae ("rumpy-riser") or several coccygeal vertebrae with severe kink ("stumpy"). Typical in Manx cats, dominant trait with incomplete penetrance for locomotor abnormalities of hind limbs. It is semi-lethal when associated with spina bifida, deformed hind limbs and pelvis, microperforate anus, incontinence and syringomyelia, enlarged bladder and megacolon.

Tail kinked,³¹⁸ usually near end of tail, recessive trait.

Congenital Abnormalities of the Urinary System

Polycystic kidneys,^{66,318} usually bilateral, due to collecting tubules failing to unite with convoluted tubules, fairly common, may develop loss of weight and uremia, probably genetic, lethal gene.

Renal agenesis,³¹⁸ usually unilateral, not uncommon, males affected more often than females, cause unknown.

Renal amyloidosis, in Abyssinian cats, possibly hereditary.^{51b}

Congenital Abnormalities of the Circulatory System

A wide variety of cardiac anomalies have been de-

scribed in the cat, as in the dog, but they are uncommon, 0.11 percent, and the cause is not determined. Some of the abnormalities described include:^{109,230,318,367b}

Aortic stenosis with enlarged left ventricle, systolic bruit.

Patent ductus arteriosus, enlarged heart, continuous bruit, possibly hereditary.

Endocardial fibroelastosis, in Siamese and others, possibly hereditary, cardiac hypertrophy, kittens grow slowly.

Persistent right aortic arch causing stenosis of the esophagus and regurgitation, corrected by incising ligamentum arteriosum.

Ventricular septal defect, probably common, enlarged right heart and thrill on palpation of sternum.

Tetralogy of Fallot, uncommon.

Congenital Abnormalities of the Digestive System

Cleft palate, often seen with other skeletal defects, in Siamese and others,³¹⁸ occasionally with hare lip, probably hereditary.

Esophageal achalasia, dilation of esophagus with regurgitation after eating, probably hereditary in Siamese cats.^{44,318} It should be differentiated from megasophagus secondary to vascular ring anomalies.

Megacolon³¹⁸ with possible absence of myenteric plexus (see Manx syndrome), unknown often lethal defect.

Portacaval anomalies with neurologic signs (hepatic encephalopathy) reported in Persian and Himalayan cats³⁶⁹ and domestic shorthair cats,^{228b} heredity unknown.

Congenital Abnormalities of the Blood

Factor VIII Deficiency, Hemophilia A in male domestic short-haired cats⁶⁰ with prolonged bleeding after surgery responding to blood transfusions, probably sex-linked autosomal recessive.

Factor XII Deficiency, Hageman Trait,¹⁹³ an autosomal recessive trait, affected animals are normal with bleeding propensities.

Congenital Abnormalities of the Skin

Skin fragility, defective collagen fibrillogenesis, cutaneous asthenia, Ehlers Danlos Syndrome,^{171b,281} is probably an autosomal dominant trait, characterized by easily stretched skin that is readily traumatized.

Epitheliogenesis imperfecta, probably rare, in Siamese,^{109,171b} possibly genetic, Lesions were on the tongue.

Rex mutant,^{171b,318} adult hair is curly, short and guard hairs and vibrissae absent or abnormal, single autosomal recessive trait.

Hairlessness, hypotrichosis, "Sphinx cat,"^{171b,318} probably a recessive hereditary defect.

Miscellaneous Congenital Abnormalities

Porphyria,³¹⁸ brownish to reddish-colored teeth, bones and urine due to overproduction of porphyrins, caused by a simple autosomal dominant trait, uncommon.

Umbilical hernia, fairly common, genetic predisposition.

Diaphragmatic hernia,^{109,318} **agenesis of part or all of diaphragm**, labored breathing, muffled heart sounds, fairly common (1 in 500 to 1,500 births), simple autosomal recessive.

Most domestic animals probably carry harmful genes in a recessive manner. For example breeding tests showed six dairy bulls selected at random carried two lethal genes, four semilethal defects and two characters causing female sterility.²⁴⁵ Probably few lethals ever reach frequencies higher than 0.10 in the general population and in most cases are at a level of 0.05 or less.³⁴⁷ In certain herds or kennels the incidence can become much higher. When a heterozygous recessive male is bred to his daughters a 7:1 ratio of normals to abnormals should be found.¹⁶⁴

The actual frequency of lethals or the genetic "load" is not known for genetic defects. To get this information would require careful postmortem and diagnostic examination of all dead or defective newborn animals and those developing possible genetic diseases later in life. When a recessive defective gene frequency of 0.50 is reached, as in achondroplastic Dexter cattle, all or 100 percent of the animals are heterozygous for the lethal gene and 25 percent of their progeny, a 3 to 1 ratio, are affected, or a ratio of 2 carriers to 1 lethal. A careful recording system for defects found in the purebred cattle breeds is highly desirable to detect carrier bulls used in artificial insemination, as well as donor cows, to prevent deleterious genes from becoming widely disseminated. This is particularly necessary when bulls used in artificial insemination are not progeny tested.

Most lethal and semilethal characters in animals cannot be detected in the heterozygous or carrier state. One of the best, but costly, way to test for carriers is test mating or progeny tests. The minimum number of progeny needed to prove with 95 percent assurance that a male is not a heterozygous carrier of a lethal trait is:^{164,347}

5 normal progeny if the sire is mated to homozygous carrier females.

11 normal progeny if the sire is mated to heterozygous carrier females.

23 normal progeny if the sire is mated to his daughters.

23 normal progeny if the sire is mated to his sibs with one parent heterozygous.

17 normal progeny if the sire is mated to his sibs with two parents heterozygous.

23 normal progeny if the sire is mated to his half sibs. Since carriers are often difficult to locate, limited progeny testing may be carried out by inbreeding a sire to his daughters or by utilizing superovulation and embryo transfer.¹⁷⁴ With a defective gene frequency of .10 in a breed or herd, random mating would produce an incidence of 1 percent defective animals. But if a carrier or heterozygous sire was used at random in these latter two populations the incidence of defective animals would rise to 0.5 and 5.0 percent, respectively. This is why it is highly desirable to mate a prospective AI stud to 200 to 600 random cows during his testing period. Adequate, prompt and complete reporting of defective calves from these matings is essential.³⁶⁷

Certain harmful traits may be spread widely if they are associated with desirable traits. This is called **pleiotropism**.³⁹⁷ For example, the simple autosomal recessive defect with incomplete penetrance of gonadal hypoplasia in Swedish Highland cattle was greatly increased by selection for the white color. In 1936 it was present in 17.3 percent of the cattle of the breed. By careful inspection and pedigree controls the condition was reduced to 9.4 percent in 1948 and 4.2 percent in 1964.²⁰ It will take many decades of careful control measures to reduce the incidence to below 1 percent of the cattle. Thus early detection and control of defective traits is imperative. To eliminate a lethal or semilethal trait in a herd it is much easier to outcross with unrelated animals. For example to reduce hermaphroditism in polled goats rapidly, a horned buck should be used. This eliminates the undesirable phenotypic character in the heterozygotes produced.

Environmental conditions may play an important role in the expression of many lethal or semilethal defects. Some animals have a recessive character but won't exhibit it unless the environment is proper. For example porphyria in cattle requires a white skin and sunlight to produce the characteristic dermal lesion. It is not unusual for a defect of one gene to produce a chain reaction in the early embryo resulting in a variety or syndrome of signs and lesions in the newborn. In reviewing the extensive lists of lethal or semilethal characters it is obvious that similar defects or homologies appear in a number of species including man.¹⁷⁷ A study of these defects in animals may thus be of benefit to the understanding of human medicine and genetics. There is no doubt but that genetics or inheritance plays an important role in the resistance or susceptibility of certain animals to bacterial, viral, parasitic diseases, tumors, metabolic and endocrine diseases. The inheritance of these characters is probably polygenic. If management, drugs, nutrition or surgery are not adequate to control the disease,

selection for disease resistance has proven of definite value and probably should be used more in animals than it is at present. Excellent discussions of the control of defective characters have been published.^{163,164,397}

Neither destroying nor ignoring defective animals is effective in eliminating a genetic problem appearing in a herd or kennel. The veterinarian should provide genetic counseling for his clients after he has mastered an understanding of genetic principles and is knowledgeable concerning the known hereditary animal diseases. According to the American Veterinary Medical Association,⁶² the performance of surgical procedures to conceal or correct genetic defects in animals to be shown, bred or sold is unethical.

"One principle is clear; it is as much the duty of the veterinarian to the community and to the state to use whatever influence and power he possesses to prevent the production of defective animals as it is to prevent the spread of infectious diseases. Each leads eventually to the same port."¹⁰⁷

Nongenetic or Congenital Defects or Anomalies in Domestic Animals

Modern teratology has largely developed within the past 40 years with the impetus of early experiments by Warkany who showed that dietary deficiencies could produce malformations; the demonstration that viral infections of the fetus (rubella) could result in defects of the newborn; and the widespread reports on thalidomide, a sedative drug, that produced many defective infants. Since then hundreds of such factors have been shown to produce anomalies in animals.³⁸⁶

Six principles of teratology have evolved that increase our understanding of teratogenic mechanisms.³⁸⁵

1. Susceptibility to teratogenesis depends on the genotype of the conceptus and its manner of interaction with adverse environmental influences.
2. Susceptibility to teratogenesis varies with the stage of development of the zygote at the time of exposure to the adverse factor. (The embryo is most susceptible during the period of organogenesis, the latter two-thirds of the embryonic period. The zygote is not as susceptible to teratogens during the period of the ovum or blastula or during the period of the fetus, especially the last trimester of gestation.)
3. Teratogenic agents or factors act by specific mechanisms on developing cells and tissues to set in motion abnormal developments. (pathogenesis.)
4. The access of adverse influences to developing tissues depends on the nature of the agent or influence, whether physical or chemical.

5. The four manifestations of abnormal development are death with resorption or abortion, malformation, growth retardation and functional deficit.
6. Degrees and frequency of deviant development increase as dosage increases, from no effect to a lethal one.

The non-genetic anomalies, or monsters, may be of innumerable types and degrees. If the malformation involves only an organ or part of the body it is called an **anomaly**; if the deformity is extensive the animal is spoken of as a **monster**. If a similar defect appears quite frequently in related individuals or those tracing back to a common ancestor, a genetic cause should be suspected. But some of these defects appearing in families or related animals in a herd may be due to environmental causes that would be impossible of differentiation without a carefully controlled genetic experiment. Many nongenetic anomalies closely resemble genetic anomalies and are called **phenocopies**. The nongenetic anomalies or monsters are caused by a variety of environmental factors or agents called **teratogens**. In recent years much basic research has been done on identifying the many factors that can effect genes or their function and produce anomalies.^{33,88,186,208,385,386,388}

The agents or factors that have been shown to be teratogenic in one or more species include the following:

Nutritional deficiencies in the dam including: vitamin A and E, riboflavin, folic acid, pantothenic acid, niacin and other vitamin deficiencies; mineral deficiencies such as copper, iodine and manganese, and amino acids such as tryptophan may cause congenital defects. Hypervitaminoses A and D will also cause anomalies in animals.^{33,186,273,385,386} For example disorders of myelination with C.N.S. signs due to a copper deficiency may cause congenital swayback of lambs and spinal ataxia of pigs.^{88,149} Vitamin A deficiency produces compression lesions of the optic nerve with blindness, and more serious anomalies in fetal pigs.^{88,273} Manganese deficiency in pregnant cows can produce skeletal deformities in the newborn calves.¹⁴⁹ Osteogenesis imperfecta in dogs has been reported to be a genetic defect but it has been shown in many instances to be a nutritional disease caused by all meat diets low in calcium.^{204,301}

Endocrine disturbances of the dam as in: diabetes, thyroid malfunction, and large exogenous doses of glucocorticoids, ACTH, insulin, androgens, progestagens, estrogens, thyroxine and thiouracil will cause defects of the embryo. Large doses of glucocorticoids in pregnant animals at the proper stage of gestation may cause cheilopalatoschisis.¹⁰² Progestogens and androgens given

during early pregnancy can cause masculinization of the genitalia of female fetuses.^{3b,69} Numerous masculinization changes were produced in female canine fetuses when the dam was given mibolerone, an androgenic steroid used to suppress estrus, during the gestation period.^{342a}

Physical factors such as: reduced atmospheric pressures, hypothermia, hyperthermia and anoxia cause anomalies. For example, hyperthermia of 2 to 3° C. for part of the day during pregnancy in sheep caused microencephaly and growth retardation. Other animals were similarly affected.^{33,88}

Radiation by X-ray or radioactive substances induces congenital defects.^{236,386}

Drugs or chemicals as: thalidomide, quinine, sulfonamides, tetracycline, streptomycin, salvarsan, lead, mercury, nicotine, malathion, carbon tetrachloride, apholate, selenium, fluorine, cytotoxic agents including aminopterin in sheep,¹⁷⁰ nitrogen mustard, actinomycin D, 6 mercaptopurine, and other new anticancer drugs, azoserine, azo dye, trypan blue and other dyes, salicylates, histamines, ergot, "Diamox," reserpine, phenylmercuric acid, galactose, E.D.T.A. and certain plant compounds as in *Veratrum californicum* and locoweeds, possibly containing lathyrogens, have all produced fetal anomalies in animals under certain conditions.^{187,190} Many new chemicals and drugs that may be teratogenic are rapidly being developed and introduced into the environment.

Further examples of drug or chemical-induced teratogenesis in animals include:

Griseofulvin therapy for ringworms in pregnant cats³³⁰ caused multiple congenital malformations of hydrocephalus, exencephaly and spina bifida in their fetuses.

Methallibure, an effective estrous cycle control agent in swine, fed to pregnant sows caused embryonic deaths when given from days 13 to 23 of gestation and after 24 days fetal pigs developed skull anomalies, alopecia and splayed legs.³²³

Trichlorfon, a parasite treatment, when fed to pregnant sows caused ataxia and tremors in piglets, resembling congenital tremors caused by viral or genetic causes.¹⁹⁶

Parabendazole, an anthelmintic, when given days 21 to 24 of gestation, produced skeletal anomalies of the vertebral column, long bones, digits and joints of fetal lambs.³²¹ This drug was not teratogenic for swine, cattle, rabbits or hamsters but was for rats.

Cambendazole (CBZ) has been reported to be teratogenic, causing limb deformities in lambs and possibly foals, when administered early in gestation when embryonic organogenesis is occurring.^{89b} Many plants, especially certain pasture plants, are teratogenic such as:

Tobacco (*Nicotina glauca*), especially its alkaloid anabasine, produced arthrogryposis and curvature of the spine in offspring of cows and sows fed tobacco 45 to 75 days and 18 to 68 days of gestation, respectively.^{33,88,187,190}

Lupine (*Lupinus sericeus*) crooked calf disease and (*Conium maculatum*) **poison hemlock** containing the alkaloid coniine, when ingested by pregnant cattle produced similar congenital arthrogryptic defects in their fetuses.^{88,93,169,188,189} The latter toxic agent ingested by sows produced congenital tremor, ataxia and arthrogryposis in their newborn piglets. Sheep were resistant to coniine and lupine teratogenicity.

Locoweed, (*Astragalus lentiginosus* and *Oxytropis*) when ingested by pregnant ewes caused wide spread neurovisceral cytoplasmic vacuolation in their fetuses,¹⁴¹ with limb and facial deformities and abortion and occasionally small weak lambs.¹⁶⁹ These plants also produced abortion and congenital limb deformities in cattle and probably horses.^{239b}

Veratrum californicum or false hellebore if ingested about 14 days of gestation by pregnant ewes causes severe skull and facial deformities including cyclopia ("monkey-faced" lambs), lack of a pituitary gland and prolonged gestation and fetal giantism. If the toxic plant is ingested from 28 to 30 days of gestation, defects in bones of the forelimb and spine of the fetus occur.^{36-38,169}

Jimsonweed, *Datura stramonium* and **wild black cherry** (*Prunus serotina*) ingested by pregnant sows was the apparent cause in two outbreaks of severe arthrogryposis in newborn piglets.²²⁴

Other plants have been incriminated or suspected of causing congenital defects.^{33,211,213} In range or pasture areas where such plants are present and causing losses, preventive measures of destroying the plants, fencing off areas where plants are present, and other pasture management practices are indicated. Also changing the time of breeding so poisonous plants are not available for ingestion at the critical stages of gestation may be helpful.

There have been several reports of extensive outbreaks of congenital abnormalities in a herd or limited area. Although conclusive proof of the etiologic agent was not obtained, plant toxins were strongly suspected.^{216,222}

Infectious agents causing fetal abnormalities are principally the viruses and *Toxoplasma gondii* that have an affinity for the central nervous system and eye.^{33,88,139} Some of the viruses that invade the embryo and fetus and produce teratologic defects are:

Togaviridae, pestivirus

Hog cholera (swine plague) virus,^{88,98,284,366} causes growth retardation, C.N.S. demyelination, tremors and ataxia in piglets.

Bovine virus diarrhea (BVD-MD) causes growth retardation, defects of the C.N.S., cerebellar degeneration, eye defects, cataracts and others in cattle, sheep and goats.^{17,185,331,371}

Border disease—growth retardation, defects of integument and C.N.S. (demyelination) in cattle, sheep and goats, in England and possibly the U.S.A.^{88,270,352} Border disease and virus diarrhea are probably due to the same agent (BVD virus) (See Abortion, Cattle, Sheep).

Rubella (measles)—multiple defects in humans.^{88,249}

Bunyaviridae, Akabane virus—multiple C.N.S. defects and arthrogryposis in cattle, sheep and goats, in Japan, Australia and Israel.^{142,166,380}

Reoviridae, orbivirus, Blue Tongue virus—multiple C.N.S. defects and hydranencephaly in sheep and cattle in Southern U.S.A. and most tropical and semitropical countries.^{88,325}

Parvoviridae, feline panleukopenia virus—growth retardation, C.N.S. defects and cerebellar hypoplasia and ataxia in cats.^{68,194}

Many of these viruses produce malformations in fetuses closely resembling those described under genetic defects for example arthrogryposis in Charolais cattle and congenital tremors in piglets.^{88,284} In the future further studies such as the latter may assist veterinarians in determining the pathogenesis of an abnormality.

Ageing of ova by delaying ovulation 24 to 48 hours was characterized by a three-fold increase in chromosomal anomalies with a higher incidence of embryonic death in rats.⁴⁵ Similarly ageing of rabbit spermatozoa before permitting them to fertilize eggs resulted in normal fertilization but greater embryonic death losses.³⁵⁴ Pregnancy in older women resulted in greater numbers of mongoloid newborn, while achondroplasia was much higher in children from older fathers.²²⁷ Thus age affects the genes and chromosomes as does other agents.²⁹⁰

Other agents not mentioned have also been shown to be teratogens. These above agents behave very similar to genes by acting at certain critical stages of development on specific tissues. Some teratogens, as x-rays, have an acute or sudden effect on the early embryo and others exert a chronic effect such as in vitamin deficiencies. Environmental factors that effect teratogenesis include the age of the embryo at time of the insult, genetic predisposition of the species, the drug or agent present, the dose, the mode of administration, rate of excretion and the presence or absence of protective factors. In humans 30 percent of congenital anomalies were genetic, 10 percent due to viral infections of early pregnancy and 60 percent due to other environmental factors.¹⁶

The noninherited teratologic defects of development may be divided into two general classes^{290,314b}

1. Those malformations due to alterations in tissue

differentiation that have arisen from a single area in the embryonic disc. Most of these are due to the local arrest in the normal process of tissue development and produce:

Defects due to excessive division—for example, polydactylia, polythelia, polydontia.

Defects due to failure of structures to fuse normally—for example, palatoschisis, cheiloschisis, cranioschisis, spina bifida, and schistosomus.

Defects due to arrest in division—for example, cyclopia; ren arcuatus or horseshoe kidney; and syndactyly.

Defects due to complete local failure of tissue growth; for example amelia or lack of limbs; ectrodactyly or absence of phalanges; vertebral or costal abnormalities; epitheliogenesis imperfecta; acrania; agnathia; and anophthalmia.

Defects due to arrest in assumption of final form or position—for example, ectopia cordis, hypognathia, and dextro-position of the aorta.

Defects in the persistence and disappearance of contiguous structures that normally follow a certain pattern—for example, the aortic arches, foramen ovale, urachus, ductus arteriosus and persistence of the median wall of the paramesonephric duct.

Defects due to overdevelopment of local tissues—for example, double-muscling, tumors such as sarcomas, hemangiomas and teratomas.

Defects due to displacement of tissue such as teratomas and dermoid cysts.

Defects due to fusion of sexual characters—such as, true hermaphrodites, false hermaphrodites, and freemartins.

Defects due to miscellaneous causes—for example, ichthyosis, chondrodystrophies, osteogenesis imperfecta, and porphyria.

2. Anomalies or teratologic defects may be grouped for naming by the organs or tissues involved.^{290,314b}

Anomalies of the heart and blood vessels are relatively common in animals. Of 159 cases of cardiac anomalies in animals, 91 cases were in cattle, 28 in horses, 17 in dogs, 8 in pigs, and 5 in cats.^{228b} Fifteen other cases in animals, most of which were in cattle were described.^{266a} The author has recorded 37 cases of cardiac anomalies in cattle in which about one-third were associated with other teratologic defects. In many animals with cardiac defects death occurred soon after birth. A few animals survived a long period due to compensatory factors. For example subaortic septal defects in some cyanotic calves cause early death, while other calves similarly affected may live for years. In cervical ectopia cor-

dis most calves die soon after birth while others survive; the author knew of one such cow that lived for 13 years.

In cattle a subaortic septal defect was found by the author in 18 of 37 cattle with cardiac aberrations. This defect was commonly associated with anophthalmos or microphthalmos and a twisted shortened tail and was seen mainly in Guernseys. Clinically the affected animals showed shortness of breath on exercise, rapid pulse rate, increased cardiac area, cyanosis, and a marked systolic bruit especially over the right side of the thorax where a thrill was often palpable. Another very common defect, observed in 12 out of 37 cases in cattle, was the transposition of the aorta into the dextroposition or Eisenmenger complex, where it arose from the right ventricle or over the right ventricle and interventricular septum. In these cases and others the left ventricle was usually very small or nonfunctional and a persistence of a foramen ovale or a subortic septal defect or both were necessary so that blood from the left atrium could get into the right ventricle. Not infrequently the ductus arteriosus was persistent. In these cases, especially with the latter defect, similar symptoms were shown but the systolic bruit was more pronounced on the left side of the thorax and a thrill was not palpable.

Other cardiac anomalies include atresia of the aorta with persistence of the ductus arteriosus; cor triloculare biatrium; tetralogy of Fallot; ectopia cordis, either cervical, pectoral or abdominal;²⁰⁵ (See Figure 52) persistence of the right aortic arch with absence of the left causing stenosis of the esophagus; and various types of acardiac monsters.

In dogs congenital heart anomalies are quite common with an incidence of about 1 percent. Since many neonatal pups die without a postmortem examination some deaths could be due to cardiac defects. Some of these defects are genetic. The most common congenital heart defects in dogs are: pulmonic stenosis, aortic stenosis, patent ductus arteriosus, interventricular septal defect, tetralogy of Fallot, persistent right aortic arch with a left ductus arteriosus resulting in compression of the esophagus and pericardial defects.^{276,395}

Cardiovascular anomalies in the **cat and sheep** are uncommon and have been reviewed.⁷⁹ Of 4,417 lambs necropsied, 401 had congenital defects and 51 or 12.7 percent had cardiac defects, most commonly septal defects. **In horses** congenital valvular defects are most common.^{228b} One foal with a persistent right aortic arch with a left ductus arteriosus has been described.^{25a} Various human cardiac anomalies have been reviewed.^{1,208} Five cases of multiple congenital heart anomalies in Arabian or half-Arabian foals were reported.^{25b}

Anomalies of the thorax and lungs are not common in domestic animals. Occasionally congenital diaphrag-

matic hernias have been described in the dog and cat¹¹³ and in cattle.³⁶² **Anomalies of the lungs** are rare in animals. Two calves with accessory lungs and one with bronchial hypoplasia and other anomalies of the lung have been described.³⁵⁶

Anomalies of the digestive or alimentary tract. The brachycephalic breeds of dogs quite commonly are affected with cleft palate and harelip or cheiloschisis. The condition results in difficulty in nursing or drinking and milk may return through the nostrils. This condition is occasionally seen in cattle and horses. A ranula or retention cyst of the sublingual or submaxillary salivary gland is observed occasionally in dogs and other animals and is usually due to injury to the salivary ducts. True branchial cysts are less frequently seen but are lined with epithelium, not granulation tissue as are salivary cysts.^{186b} These cysts are probably due to an anomaly in the development or regression of branchial duct II, pharyngo-branchial duct II and the cervical vesicle. Severe anomalies of the face, head and thorax, obstruction of the esophagus or high intestinal obstructions in monster fetuses are often associated with hydramnios. No meconium is normally evacuated during intrauterine life except when the oxygen supply is reduced. With anoxia the fetus becomes distressed and the anal sphincter relaxes.²⁹⁰ Atresia ani is seen in all domestic animals but most commonly in swine. It may be a genetic defect. In females the anus is imperforate but often a union with the urinary and genital structures has occurred, resulting in a common cloaca.

Abdominal hernias such as umbilical hernias are due to failure of the normal closure of the abdominal ring and may also be genetic in nature. The liver is seldom affected by anomalies except for cysts often seen in cases of bovine *Schistosomus reflexus*. Congenital diaphragmatic and peritoneopericardial diaphragmatic hernias have been reported.¹⁰⁶

Anomalies of the urinary system are not uncommon. Polycystic kidneys are seen in almost all domestic animals, especially swine and cats and may be genetic. Fusion of the caudal poles of the kidneys, ren arcuatus, to form a single horseshoe-shaped kidney is occasionally observed especially in monster fetuses. Occasionally marked hypoplasia of one or both kidneys may occur, or in rare cases one or both kidneys may be absent, unilateral or bilateral agenesis.²⁵⁰ Stenosis due to local muscle hypertrophy of the ureter at the bladder, atresia of the ureters or ectopic ureters will cause cystic dilation, hydroureter and hydronephrosis. Dogs with ectopic ureters opening into the vagina or vestibule result in constant dribbling of urine from the vulva.² A similar condition has been observed by the author and others^{316a} in

a mare and a yearling filly. An ectopic ureter in a heifer that opened into the urethra caused incontinence.⁴⁹ A rare ectopic ureter in a male dog that terminated in the urethra²⁶⁸ has been reported. Other congenital anomalies of the urinary system in the dog and cat have been reviewed. In occasional instances the urachus fails to close at birth, resulting in a persistent dribbling of urine from the navel. This is seen most commonly in foals, but also in cats and other animals.

Anomalies of the genital organs and gonads will be discussed in future chapters on infertility in female and male animals.

Mammary gland anomalies include fused teats and supernumerary glands and teats. Some of the supernumerary teats, polythelia, may be fused to the normal teat. The mammary glands in virgin animals may enlarge and secrete a small amount of milk during gestation due to the effect of hormones from the placenta, from the ovary, from granulosa cell tumors or by ingestion of estrogenic mycotoxins. Congenital atresia, or stenosis of one or more teats or glands, may occur but this is difficult to differentiate from pathological processes that may have occurred prior to or after parturition. A rare case of total mammary gland aplasia was reported in a fertile cow.¹¹⁵

Hermaphroditism or intersexuality occurs most commonly in goats and pigs, and less commonly in horses and dogs. It is occasionally present in sheep and cattle and is rare in the cat. **Intersexes** are individuals in which the diagnosis of the sex is confused because of congenital anatomical variations and abnormalities of the genital organs. Conditions in intersexes include hermaphroditism, abnormalities of the accessory genital organs, gonadal dysgenesis, and freemartinism.^{35,238} These latter two conditions will be discussed later.

Pseudohermaphrodites occurred in 11.1 percent of Saanen and 6 percent of Toggenburg goats.⁹⁵ This figure may reach 14.9 percent in certain herds, with a sex ratio of 55.1 percent males, 30 percent females and 14.9 percent pseudohermaphrodites.¹² Thus these caprine pseudohermaphrodites, even though they have testes, are female according to the sex ratio, sex chromatin studies and chromosome analyses. In goats this condition is a simple sex-limited recessive character associated with hornlessness or the polled condition. Horned hermaphrodites are extremely rare. A similar recessive type of hermaphroditism in swine was described and in an inbred swine herd where 106 pigs in 11 litters were sired by a single boar there were 68 males, 22 females and 16 intersexes.^{123,288} Some hermaphrodites may be nongenetic.

A study of 48 naturally occurring and 52 drug-induced canine hermaphrodites showed 33 percent of the former were Cocker Spaniels. Evidence indicated that some of

these might be caused by a single autosomal recessive gene. Of the natural hermaphrodites 25 were male pseudohermaphrodites and 13 were true hermaphrodites. All dogs in this study had either an enlarged clitoris or an underdeveloped penis.^{139b} A specific type of male pseudohermaphroditism has been described in Miniature Schnauzers characterized by persistence of the Mullerian ducts (uterus), cryptorchidism and subsequent signs of Sertoli cell tumors and endometritis.^{203b}

Intersexes may be separated into males or females based on (1) their genetic sex, either chromosomal or nuclear sex, (2) their gonadal sex or presence of ovaries or testes, (3) their phenotypic sex or the morphology of their accessory genital organs, and (4) possibly their hormonal or behavioral sex.¹³⁷ Hermaphrodites are usually classified on the basis of gonadal sex with **true hermaphrodites** having both testes and ovaries or ovotestes and **pseudohermaphrodites** having gonads of only one sex. **Male pseudohermaphrodites** phenotypically resemble females but have testes and **female pseudohermaphrodites** resemble males but have ovaries. Some workers prefer to consider the terms true hermaphroditism and pseudohermaphroditism as misnomers indicating they should be regarded as degrees of intersexuality.

The true hermaphrodite is rare and has internal genitalia resembling both sexes and external genitalia of an intermediate type that may tend either toward the male or female. True hermaphrodites are reported most frequently in swine and occasionally in dogs.^{350a} In most cases the genetic sex is female (XX) but it is likely that on further study many of these cases may prove to be mosaics or chimeras produced by nondisjunction and/or other mitotic errors during mitosis early in embryogenesis or dispermic fertilization of an ovum by an X-bearing sperm and a nonextruded polar body by a Y-bearing sperm resulting in tissues with variable sex chromosome complements such as: XX/XY, XXY, XXYY or XXXY and etc. Two such cases of true hermaphrodites in cattle were described as occurring in single born animals; one had XX/XY and the other XX/XXY cell types especially noted in the kidneys and gonads. Both cattle appeared to be males with a penis but no testes in the scrotum. On internal examination one had an ovary and an ovotestis; the other had a normal ovary and a very undeveloped gonad consisting of primitive medullary tissue. Both had a fairly well developed uterus.^{89c}

The female pseudohermaphrodite is also rare in animals. Intersexes with female gonads and external genitalia resembling the male may be produced by exposure to androgens during embryonic life. This might be caused by a lesion of the adrenal gland or a biochemical lesion of steroidogenesis. Female or true hermaphrodites with

fairly normal external and internal female structures may rarely be fertile since ovulation may occur.¹⁵⁶

The male pseudohermaphrodite is most common with testes in the abdominal cavity or beneath the skin in the scrotal region. (See Figures 35, 36, 37.) The scrotum seldom develops in these animals, due to the anomalous growth of the external genital organs which usually resemble the female. Often a greatly enlarged clitoris is present, which with the vulvar configuration is called "fishhook" vulva in swine. This often causes these animals when urinating to direct the stream in a greater dorsal arc than does the normal female. The location of the urethral opening may be anywhere from that of the normal female to one in a penis-like structure with hypospadias in the scrotal or abdominal region. If animals possessing these abnormal characters resemble the female sufficiently to deceive the owners, they may be detected by their failure to show signs of estrus, and by



Figure 35. False masculine porcine hermaphrodite—note testes, uterus, and "fish hook" vulva.

their body appearance of a male castrate. Hermaphrodites commonly resemble cryptorchid males in their male actions and attitudes. In the male pseudohermaphrodite the internal genitalia resemble both sexes and a uterus-like structure is nearly always present. Hermaphrodites are invariably sterile, especially males with intraabdominal or subcutaneously located testes. Almost all male and female pseudohermaphrodites are genetic or chromosomal females (XX) and are positive on nuclear sexing as indicated by the presence of the sex chromatin mass or Barr body in the nucleus.

The technic of nuclear sexing consisting of examining certain somatic cells of animals for the presence of the inactive X chromosome in the nucleus has been described.^{14,246b,342} Cells from various tissues that are most satisfactory to examine will differ from species to species but buccal epithelium, nerve cells and polymorphonuclear neutrophils are most commonly utilized. The Feulgen staining method is highly satisfactory after the



Figure 36. False masculine bovine hermaphrodite—The testes were beneath the skin in the inguinal region.



Figure 37. False masculine equine hermaphrodite—This horse behaved like a stallion.

cells are fixed. The cells are examined for a dark-staining, small, about 0.8 by 1.2 micron, planoconvex mass or body against the inside of the nuclear membrane. In neutrophils this body is observed as a similar-sized small projecting mass, a sessile body or "drumstick," attached by a small stalk to the nucleus. These sex chromatin masses or Barr bodies, named after the person who first described them, are observed in most female cells examined and are absent in the cells of males. Thus females are sex chromatin positive and males are sex chromatin negative. In female or male cells with abnormal numbers of sex chromosomes, XXX, XXXY, and etc., the number of Barr bodies observed is always one less than the number of X chromosomes. Although nuclear sexing is a very helpful and simple technique, examination of the chromosomes by karyotyping is more accurate and informative especially for the determination of the true chromosomal complement of intersexes.



Figure 38. Diphallus or double penis in a bull.

When gonadal tissue in the embryo remains undifferentiated, undeveloped, is absent, or is surgically removed early in embryonic life, the internal and external genitalia become female in character. The Y chromosome is apparently necessary to initiate the development of the testis and then the testicular androgen secretions, and cause the development of the external genital organs characteristic of the male animal. An individual with XXY or XXXY chromosome make-up will have a male phenotype but he is sterile. In humans and animals extensive cytogenetic studies have been conducted on these XXY individuals with Klinefelter's syndrome. The testes are very undeveloped and hypoplastic and few or no spermatozoa are produced. This syndrome has been described in human males, in tortoise-shell male cats and in boars, rams, dogs and bulls.⁹¹ In another common chromosomal deficiency in humans and animals called Turner's syndrome the Y chromosome is missing. The human or animal which has an XO chromosomal complement is a short, small female with undifferentiated rudimentary gonads or gonadal dysgenesis.^{10,64b,154,342} In male pseudohermaphroditic swine, and the same is true in goats where this condition is also genetic, cells have only an XX chromosome complement.¹²³ Pseudohermaphroditism in swine, goats and dogs may be inherited as an autosomal or sex-linked recessive gene or a dominant gene with incomplete penetrance.^{281,300} Hypoplastic testicular development with modification of the external genital tract occurs in the absence of the Y chromosome. Autosomal modifiers in this sex-linked recessive condition might cause the development of the testes.¹²³ Injections of male sex hormones into the dam during gestation will cause modification of the external genitals of a female fetus in the male direction.⁶⁹

Recent studies^{89d,161,201,335,370} have indicated that a cell

surface component recognized serologically as H-Y antigen governs the development of the initially indifferent gonad, early in embryonic life, toward the male or testicular mode in species in which the male is the heterogametic sex. Although the H-Y gene is probably on the Y-chromosome, there are studies to show this gene may be on the X-chromosome or on an autosome. It possibly requires a male hormonal environment for its expression. It has been proposed the H-Y gene and two other genes, one that activates the H-Y structural locus and the second that codes for specific H-Y antigen receptors, may be required for testicular differentiation. After the initial differentiation of the gonad into a testis, the latter produces androgens which cause virilization of the accessory glands, ducts and external genitalia. The fetal testes also secrete a paramesonephric (Mullerian) duct inhibiting factor or antimullerian hormone, possibly from Sertoli cells, suppressing the development of the uterine tubes, uterus and cephalic portion of the vagina.

These and other studies have helped to elucidate the complex factors in the development and manifestation of characters associated with true hermaphrodites, pseudohermaphrodites, freemartins, and feminizing or masculinizing syndromes. In freemartins it is presently postulated that H-Y antigen produced by the male twin is carried to the female twin by the blood stream through placental anastomoses. This causes virilization of the gonad with the subsequent alterations of the genital structures to produce, in the genetic female bovine fetus, the freemartin condition.

Amniocentesis to collect amniotic fluid and cells for diagnostic analysis has been commonly performed in humans early in gestation to detect suspected fetal aberrations, or for sex determination. However in animals amniocentesis has only been performed in a limited manner and further studies and improvements are necessary to avoid fetal deaths and make the procedure more practical.⁹⁴

Hybrids are an extreme outcross, such as a cross of the ass on the mare to produce the mule or the sheep on the goat, the dog on the coyote, and the bison on the cow.

The ass-mare or stallion-ass breedings produce mules or hinnies, respectively.³³⁷ These hybrids are the only commercially-produced man-made animals and they are always sterile. Workers in the field of cytogenetics have been making interesting studies on these hybrids.³⁰ The ass with a diploid chromosome number of 62 when mated with the horse with a diploid chromosome number of 64 produces a mule with the chromosome number of 63. The female mule has a normal ovarian hormonal function producing normal follicles and corpora lutea, ex-

inhibiting estrus and occasionally showing mammary development with the production of milk. However, because of the very limited number of oocytes in the ovaries, estrous cycles may be of a normal length (22 days) or with long periods of anestrus between estrous periods. The female and male mules are sterile, probably due to a failure of gametogenesis caused by asynapsis during the first meiotic division. A number of alleged fertile female mules examined were found to be donkeys rather than mules when chromosome studies of their body cells were made.³¹ In the male mule a few spermatozoa may be found but they are smaller in size than those from a normal stallion or ass, possibly being quasi-haploid. Other interesting facts concerning this hybrid are that in female mules or hinnies the donkey x chromosome, of the two x chromosomes present in each cell, is inactivated. The production of PMSG from the endometrial cups in pregnant mares with horse fetuses and donkeys with donkey fetuses is high as it is in donkeys carrying hinnies. But in mares carrying mules very little PMSG is produced.³³⁷ Recent unpublished investigations at Cambridge and elsewhere into the immune phenomena occurring during early pregnancy, occasioned by the intimate association of a foreign fetal placenta with the maternal endometrium, are being studied by newer immunological and biological techniques involving hybrids of donkeys and horses and sheep and goats. For example donkey embryos transferred into mare recipients are rejected and aborted after developing to about 90 days of age; while horse embryos transferred into donkey recipients are carried to term.^{8b}

Forty-five percent of does bred to rams and ewes bred to bucks conceived, however nearly all aborted before 145 days.^{34,43} The diploid chromosome number of sheep is 54, goats 60¹⁵ and their embryonic hybrids was 57.



Figure 39. Hydrocephalus in a feline fetus.



Figure 40. Anasarca or edema of a canine fetus.

Production of hybrids from sheep and goats was reported and reviewed.⁴³ Both the dog and coyote have similar karyotypes with 78 chromosomes each and although many believe these hybrids may produce fertile offspring further experimentation is needed. Dystocia occurring at the birth of the hybrid fetus produced by mating a bison bull with possibly 60 chromosomes with a domestic cow having 60 chromosomes was due to the severe amnioallantoic dropsy regularly present.³⁸³ Beefalo bulls with more than three-eighths bison "blood" when bred to domestic cows often produce pregnancies with dropsy or abortion.⁴⁷ Further study is also needed with this hybrid to determine the mechanisms involved in the abnormality.

Anomalies of the head and central nervous system may include:

Microcephalus is characterized by a small cranial cavity and brain.

Cyclopia or cebocephalus is characterized by a single orbit in which global tissue is absent or rudimentary or in which the eyeballs vary from a single apparently normal eye through all degrees of doubling to one consisting of two complete but small adjacent globes (See Figures 41 and 42). Eyelids are rudimentary or absent and the nose is usually absent or in the form of a tubular appendage placed above the centrally located eye. This rudimentary nose does not communicate with the pharynx. The skull is usually small and the lower jaw, being longer than the defective upper jaw, is curved dorsally at its cranial end. Cyclopia is seen most commonly in the pig and sheep as a congenital but nongenetic defect but may be present in all species.

A congenital malformation of sheep affected 1 to 8 percent of the newborn lambs in flocks in southwestern Idaho. It was characterized by cyclopia or a "monkey-faced" condition, harelip, cleft palate, hydrocephalus,

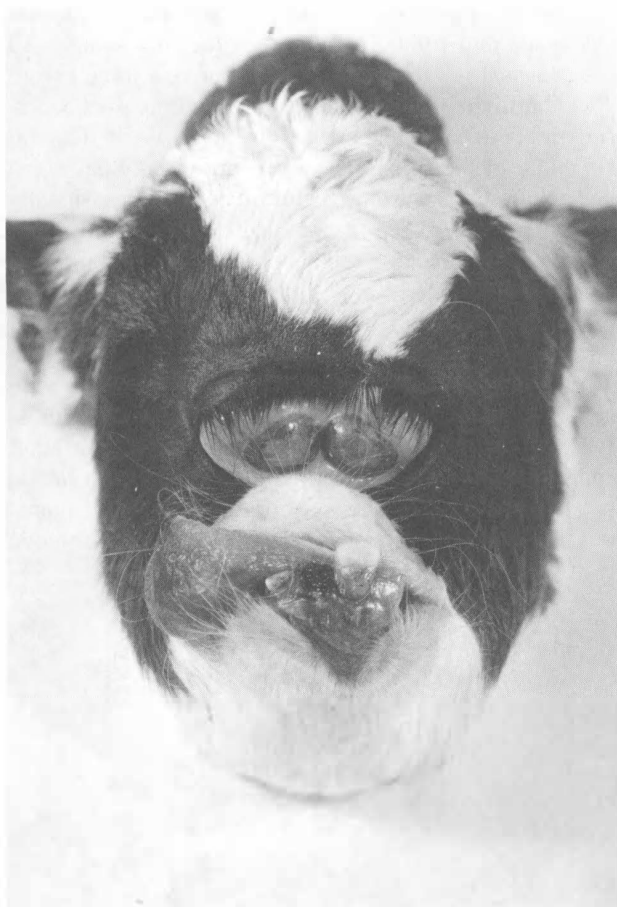


Figure 41. Cyclopia or cebocephalus in a Holstein calf.

short upper jaw, prolonged gestation of 200 days or more with fetal weights up to 20 lbs., associated with involution of the mammary gland, a small dark vulva, and occasionally rupture of the prepubic tendon due to the large size of the fetus or fetuses.^{36,37,38} This condition was not due to a genetic character. Head defects were severe in the overtime fetuses. The pituitary gland or hypophysis was absent or grossly defective. Subsequent work showed the cause of this condition to be the ingestion of *Veratrum californicum* between 8 and 17 days and later the critical day was found to be the 14th day of gestation. If the feeding of this plant was continued after the 15th day, embryonic death apparently occurred in a high percentage of ewes. If flocks were on range containing this plant, the incidence of "dry" or barren ewes at lambing could be 10 to 15 percent rather than the normal 1 percent. The teratogenesis of this condition has been described.¹⁰²

Hydrocephalus is due to an abnormal accumulation

of fluid in the cranial cavity. Internal hydrocephalus is due to excessive fluid in the ventricular system. External hydrocephalus is rare and due to excessive fluid between the brain and dura mater. Internal and external hydrocephalus may be combined. About 99 percent of human cases are caused by an obstruction to the passage of the cerebral spinal fluid into the arachnoid spaces usually due to an associated spina bifida in the fetus.²⁹⁰ In severe cases the dorsal portion of the brain is encompassed only by the skin, the subcutaneous tissues, and the brain coverings. (See Figure 39.)

Cranioschisis or crania bifida are defects of the skull that may result in meningocele or meningoencephalocele. In the later instance the skull defect is large, so that parts of the brain and the meninges are extruded.

Anomalies of the head—Facial fissures include palatoschisis, cheiloschisis, macrostomia, and schistoprosopus or divided face. Lack of cranial or facial structures include acephalia, or absence of a head; acrania; hemicrania; astomia; microstomia, arhinencephalia or absence of a nose, agnathia, hypognathia, anophthalmos, microphthalmia, aprosopia or partial or complete absence of a face, anotia or absence of ears, polyotia and polydontia or anodontia. Congenital defects of the head and ears of ovine fetuses are common. (See Figure 53.)

Anomalies of the skeleton—No genetic cause was suspected for the commonly observed condition of "contracted" newborn foals.³¹¹ Mild cases might be associated with intrauterine crowding. In most cases the characteristic anatomical changes were hypoplasia of the intervertebral articulations, hypoplasia and twisting of the long metacarpal and metatarsal bones and asymmetry of the cranial skeleton. The cause is unknown. An iodine deficiency might be associated with goiter and angular limb-deformities.^{241,242} Four mares

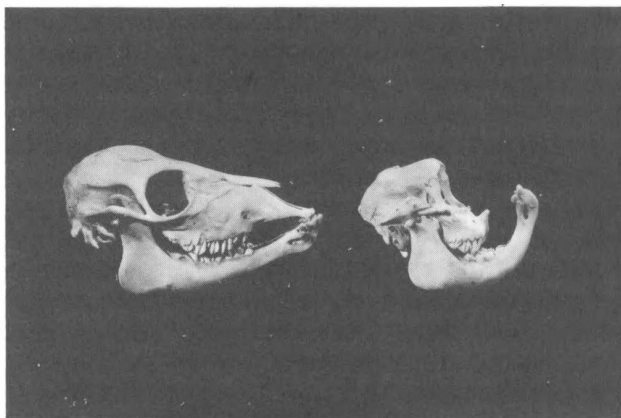


Figure 42. Skulls of normal and cebocephalic calves.

grazing Sudan pasture early in gestation, about 20 to 50 or more days, delivered dead foals with ankylosed extremities at term. Evidence of a toxic reaction to Sudan pasture with cystitis and ataxia have been reported in adult horses.²⁹²

These anomalies of the central nervous system are often characterized externally by ankylosed joints, deformed fetlocks or "club feet" and other defects including hydramnios in some severely affected bovine fetuses. As with other markedly defective fetuses their size is usually smaller than normal due to growth retardation.

Achondroplasia, chondrodystrophy or dwarfism—There are apparently several types and degrees of the defect and most, or all, are hereditary. In achondroplastic fetuses the long bones are abnormally short. The trunk is of normal length and the abdomen is large. The head is moderately enlarged and flattened. "Bulldog" head and brachygnathism of the maxilla, "undershot," and prognathism of the mandible, "overshot," are common. In Herefords, the recessive gene for dwarfism is commonly found in the heterozygous "comprest" animal. Most dwarfs are the result of a complex mode of inheritance. (See genetic bovine defects.)

Spina bifida, rachischisis or spinal dysraphism is the absence of dorsal portions of the vertebrae or vertebral arches often in the lumbar or sacral region with defective rear limbs and tail and paralysis of the rear parts. It may be occult or a skin defect may be present. It is seen in Angus, Holsteins, Bull Terriers and other animals. The anomaly may resemble the *Perosomus elumbis* monster.

Absence of the tail, anury or *Perosomus acaudatus* is seen as a common defect in dairy and beef cattle and Manx cats characterized by a lack of coccygeal vertebrae and deformed sacral vertebrae with a sunken perineal region and in some cases a characteristic hopping gait. The condition could not be proven to be genetic in nature in cattle.^{126,161}

Hemivertebrae have been seen most commonly in English Bulldogs and Boston Terriers resulting in failure of the centers of ossification to unite. **Scoliosis**, kinked tails and a shortened spine are present if many vertebrae are involved.⁹

Anomalies of the trunk—*Schistosomus reflexus* is seen most commonly in cattle but may be observed rarely in sheep, goats,^{28,77,79} and swine. It is characterized by a marked ventral curvature of the spine so the occiput of the head lies near the sacrum. The body and chest walls are bent laterally and dorsally and the thoracic and abdominal viscera are exposed. The pelvis is deformed. The liver is abnormal in shape and cystic. The rumen is

occasionally distended with fluid. The limbs are usually ankylosed and rigid. In rare cases the limbs and head may be enclosed in a complete sack of skin. (See Figure 43.) ***Campylorrhachis scoliosa*** is a fetal monster occurring rarely in cattle and swine, characterized by a lateral curvature of the spine. The limbs are usually deformed and ankylosed. ***Perosomus elumbis*** is seen occasionally in cattle, swine, sheep, and dogs and is characterized by a lack of vertebrae and spinal cord caudal to the thoracic region. The monster has a small, flattened, deformed pelvis with strongly ankylosed and flexed hindlimbs and atrophy of the muscles of the real quarters (See Figure 44) ***Perosomus horridus*** is a bovine fetal monster with generalized, severe ankylosis and muscle contractures. It is characterized on external examination by a short spine. This is due to a marked double S-shaped lateral twisting of the vertebrae. (See Figure 45.) Fetal monsters may be present with a normal, probably dizygotic twin.

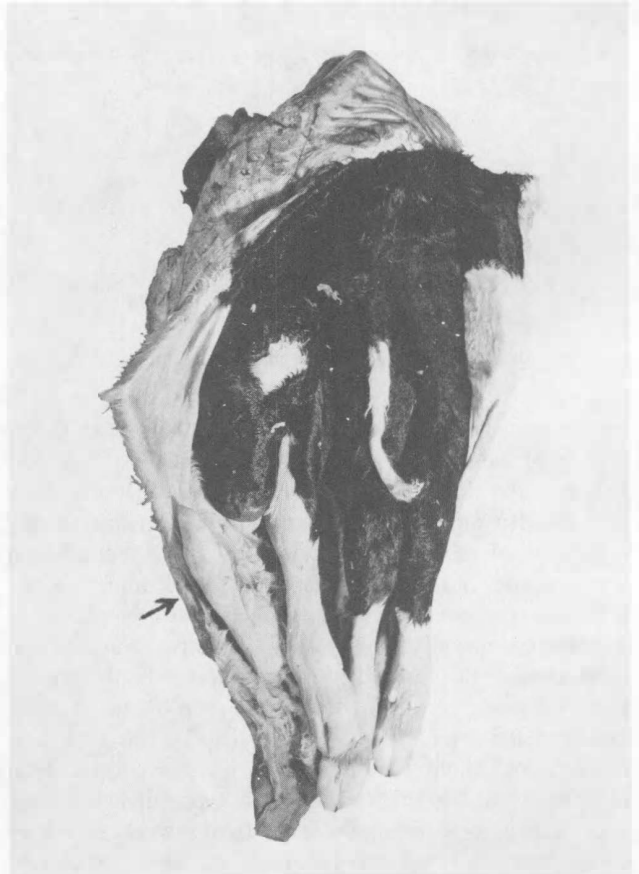


Figure 43. A bovine *Schistosomus reflexus* monster. This is an unusual type in which a sac of skin encloses the entire fetus. Note accessory limb attached to skin.



Figure 44. **Perosomus elumbis**, note lack of development of the caudal part of body and ankylosed rear limbs.

Anomalies of the limbs include amelia, missing or “amputated” extremities; (See Figure 54) micromelia; hemimelia or absence of the distal half of the limb; sire-nomelus, or fusion of the hind limbs with varying amounts of hypoplasia and deformity of the pelvis and pelvic organs; hypoplasia of the extremities; polydactyly, syndactyly; and ectrodactyly or absence of phalanges. Amelia or hemimelia were characteristic congenital defects in thalidomide toxicity in humans. Ectopia of the patella has been reported in cattle, dogs and horses.¹⁰⁸

Miscellaneous anomalies due to displacement of tissues include **teratomas**, **dermoids**, and **dentigerous cysts**. The last condition, characterized by a displaced dental follicle containing fluid and teeth, is seen most commonly in the horse. These dentigerous cysts may be located beneath the ear and are called an “ear tooth.” Dermoids are seen occasionally on the cornea, third eyelid or on the neck in cattle and other species. In horses dermoid tumors may rarely involve the ovary or testis, especially the retained testis. Teratomas are occasionally seen in all species.

Embryonic duplications are malformations due to abnormal duplication of the germinal area giving rise to fetuses whose body structures are partially but not completely duplicated. Embryonic duplications, although rare, occur most commonly in cattle and can result in severe dystocia. Whether they are caused by environmental or genetic factors or both is not known. Embryonic duplications include:²⁹⁰

- A. Free monozygotic or dizygotic twins or triplets
 1. Symmetrical twins are either monozygotic or identical, or dizygotic or fraternal.
 2. Asymmetrical twins consist of a normal and an acardiac or monster individual. These may include three types:

Hemicardius is a very imperfect individual but



Figure 45. **Perosomus horridus**. The spine has many lateral bends and all joints are functionally ankylosed.

parts are recognizable and a rudimentary heart is present.

Holocardius acephalus—The cranial portion of a very imperfect individual is lacking. No heart is present. (See Figure 50.)

Holocardius amorphus or **Amorphus globosus**—The general body form is unrecognizable. It may occasionally be seen, most

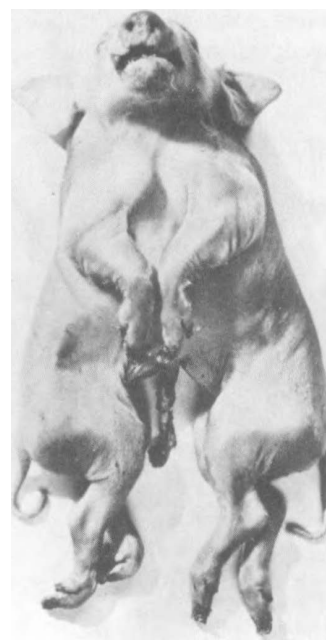


Figure 46. Porcine double monster, monocephalus tetrapus tetra-brachius.

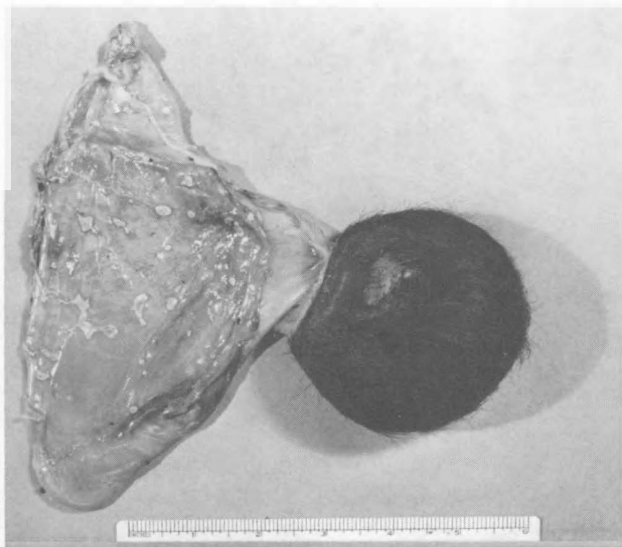


Figure 47. **Amorphus globosus** attached to the bovine fetal membranes.

commonly in the cow, but also in the mare, ewe and goat, attached to the placenta of the normal monozygotic or dizygotic twin. These very imperfect zygotes are parasitic upon the placenta of the normal twin and are never observed in single births. The bovine **Amorphus globosus** usually appears as a round or oval, edematous structure weighing 1/2 to 7 lbs. covered with skin and hair and con-

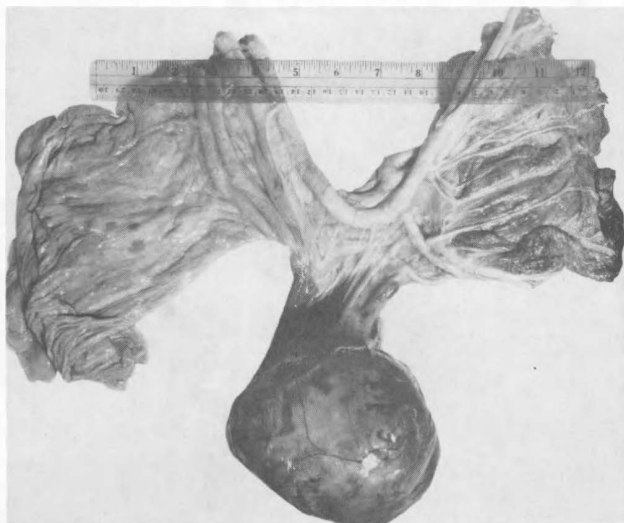


Figure 48. An ossified remnant of the yolk sac in a mare's placenta. A thin cartilaginous shell surrounds a gelatinous mass.

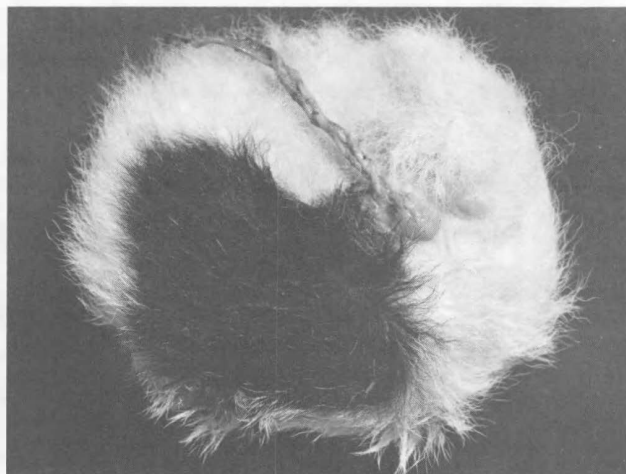


Figure 49. A bovine **Amorphus globosus** attached by a stalk containing blood vessels to the placenta of a normal fetus.

taining connective tissue, fat and other soft tissue and occasionally cartilage and bone. In the mare a rare structure consisting of a round, thin, fenestrated ball of cartilage 3 to 5 inches in diameter is covered with mucous membrane. This is not an amorphus globosus but is an ossified remnant of the yolk sac. (See Figures 47, 48, 49.) The interior of this cyst-like structure is jelly-like tissue.

In humans an amorphus structure is observed in the chorion in about 1 in every 100 single births.^{184a} Based on karyotypic studies of chromosomes, human acardiac monsters were found to be the same sex as their normal twin supporting the theory of their monozygotic origin.



Figure 50. A holocardius bovine monster without a heart. Note the imperfect face, muzzle, teeth and a tail.



Figure 51. A parasitic limb, notomelus, attached to a calf.

However, three acardius twin-bovine monsters were the opposite sex from their normal cotwin.⁹⁰ This supported Williams³⁸³ theory that the **Amorphus globosus** was an imperfect zygote of dizygotic twins. It was demonstrated that the leucocytes of the normal male calf only contained the XY or male chromosome complement and no blood cell chimerism occurred. Chromosomal analysis of an ovine acephalic acardiac monster expelled with two normal male lambs revealed a chromosome aberration, increased hypodiploidy.⁹² The monster composed mainly of stomach and intestinal tissues was enclosed in its own amnion. Another case²⁵² where two acardiac monsters were attached to the placenta of a normal bovine calf was described. The author has observed a placenta of a normal calf containing six teratomatous growths.

B. **Conjoined twins** in which the components or component parts are symmetrical are called **Diplopagus** monsters or "Siamese" twins. **Triplopagus** monsters are extremely rare. Conjoined twins arise from a single ovum



Figure 52. **Ectopia cordis** in a calf, with the heart beneath the skin ventral to the neck and cranial to the thoracic inlet.

and are monozygotic.^{11,138} They occur about once in 100,000 bovine births. They are most common in cattle but are seen rarely in sheep, pigs, dogs and cats and are rare in horses.^{15,215}

1. Those conjoined twins in which each component is complete, or nearly so, include:

Thoracopagus, sternopagus, or ziphopagus twins are joined at or near the sternal region. The internal organs are usually duplicated. The components are face to face.

Pygopagus monsters are connected at the sacrum and the components are back to back.

Craniopagus twins are united at the heads. Components may be facing in the same or in the opposite direction.

Ishiopagus fetuses are joined at the lower pelvic region and the bodies extend in a straight line and the heads in opposite directions.

2. In this group the two components equal one another but each is less than an entire individual. This is usually associated with lateral fusion. These may vary from single normal individuals to those of two normal but superficially joined individuals. Duplication may lead to doubling of the cranial end of body while the caudal end remains single; or the caudal part may be doubled and the cranial part single. Duplication can occur at both cranial and caudal ends with the middle area of the monster remaining single. Duplication of the cranial part of the fetus is more common than that of the caudal portion.

- a. Duplication in the cranial region. (See Figure 46.)

(1) **Monocephalus** includes those monsters with partial duplication of the frontal region, nose and mouth called **Diprosopus** or double face.

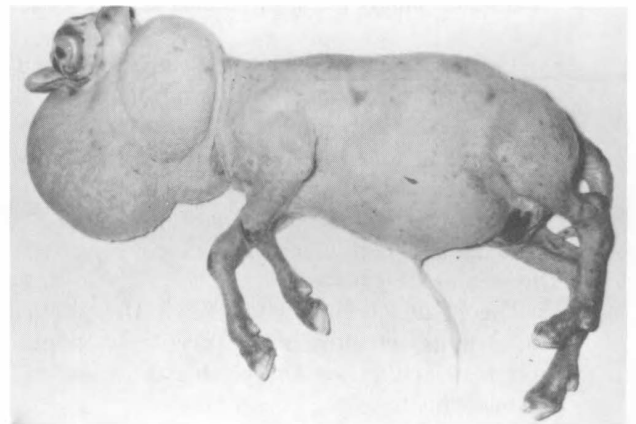


Figure 53. An ovine monster twin to a normal lamb—A cystic esophagus, agnathia, cyclopia and microcephalia were present.



Figure 54. Amelia in a Jersey calf—A portion of the humerus and the distal portion of the left forelimb was missing at birth.

Either face may be complete or one eye of each may be fused into a common medial orbit. **Di-, tri- or tetraophthalmos** and **di-, tri- or tetraotus** may be present.

- (2) **Dicephalus** or two heads, with **distomus** or **monostomus** occasionally is seen. **Tricephalus** is very rare. A **Dicephalus dipus dibrachius** monster has two forelimbs and two hind limbs with partial duplication of the spine and one or two tails, **dicaudatus**. **Dicephalus dipus tribrachius** has 3 forelimbs; **Dicephalus dipus tetrabrachius** has 4 forelimbs.
- b. Duplication in the caudal region is designated as **Dipygus**. **Tripygus** is very rare.
 - (1) **Monocephalus tripus dibrachius** has 3 rear limbs.
 - (2) **Monocephalus tetrapus dibrachius** has 4 rear limbs.
 - (3) **Cephalothoracopagus** has a single neck and more or less complete fusion of the heads to form an almost single face. **Syncephalus** has one face, four ears, and a single or partially doubled cerebrum. **Janiceps** is a monster with two faces on opposite sides of the head.
- c. Duplication of both cranial and caudal regions is **Dicephalus dipygus**.
 - (1) **Dicephalus tripus tribrachius**, **Dicephalus tetrapus tetrabrachius**, **Dicephalus tripus tetrabrachius**, or **Dicephalus tetrapus tribrachius** have been described.

C. **Unequal and asymmetrical conjoined twins** are composed of one very imperfect and incomplete twin, called the **parasite**, dependent on the other twin, the **au-**

tosite. This is called a **heteropagus monster**. The autosite is nearly normal and the parasite is attached to it as a dependent growth. (See Figure 51.)

1. The parasite may be attached to the visible surface of the autosite. Common junction sites are the back (notomelus) thorax, sacrum or pelvis, and in rare cases the abdomen, head, or buccal cavity. The latter is called **epignathus**. Five cases of notomelus in heifer calves were reported.²¹⁵ Some of the smaller, more imperfect parasites may be called **teratomas**.

A parasite can rarely develop within the autosite usually in the abdominal, thoracic, pelvic or cranial cavity, or in the spinal canal or scrotum. **Teratomas** in the abdominal cavity and between the mandibles were described in two calves.^{148b}

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Chapter IV

PHYSIOLOGY OF THE GESTATION PERIOD

In this chapter the estrous cycle, estrum, ovulation, and fertilization are purposely omitted inasmuch as they will be discussed later in Chapter XII on Physiology of Reproduction.

Shape and Location of the Pregnant Uterus

In all domestic animals as pregnancy progresses the uterus with its contents moves forward and downward in the abdominal cavity. In the cow and mare the uterus rests on the abdominal floor beneath the intestines after the fourth or fifth month of gestation. In the ruminant the uterus is usually located on the right side of the abdomen because the left side contains the rumen. In advanced pregnancy in the cow and mare the length of the fetus may exceed the distance from the diaphragm to the pelvis. In the mare this often results in the uterus and fetus assuming a diagonal position in the abdominal cavity. In the cow, in the last month of gestation, the nose and the forefeet of the fetus, together with the enveloping uterine wall and fetal membranes, may enter the pelvic cavity and extend caudally over the cervix.

The mesometrium, or broad ligament, attaching the lesser curvature of the uterus of the cow to the caudal lateral flank and pelvic regions, is stretched and pulled forward by the weight of the gravid uterus. However the ovary is never further than 20 to 25 cm. from the pelvic brim. The uterus of the cow is cornuate in shape and conical, with its greatest diameter from the cervix through the middle of the horn containing the fetus. The distal third of the horn narrows rapidly toward the apex. The opposite nongravid horn in both the cow and mare remains relatively small even though fetal membranes extend into it. These characteristics of the uterus in the cow facilitate torsion of the uterus.

In the mare the mesometrium is attached to the dorso-lateral aspect of the uterus and dorsally to the sublumbar and dorsal pelvic regions. As the uterine weight increases the ovary is pulled ventrally, but seldom more than 25 cm. from the lumbar vertebrae; the ovary can frequently be felt per rectum for much of the gestation period. The apices of the horns are directed dorsally by

the attachments of the mesometrium. The body and the horn containing the fetus are tubular and about the same diameter from the cervix to near the apex of the horn.

In the ewe the shape and location of the pregnant uterus is similar to that of the cow. The frequent incidence of bicornual twin pregnancy and the relatively smaller abdominal cavity in the ewe may be a factor in preventing uterine torsion.

In multiparous animals, as the bitch, queen and sow, the gravid horn is tubular and about the same diameter its entire length. The fetuses are usually nearly equally distributed between each horn. The horns become very long in the sow. Each pregnant horn may be 1.8 meters in length. They rest on the floor of the abdominal cavity in a folded manner, similar to intestines.

In the cow twinning usually results in bicornual twins, one fetus developing in each horn. In about 10 percent of twin pregnancies, both twins develop the same horn, unicornual twins. In these cases the horn containing both fetuses is very long and is bent at an 180° angle at the diaphragm, with one fetus lying parallel to the other. The fetus in the apex of the horn may be delayed in its expulsion at parturition or be overlooked.

Rectal examination of the cow during gestation often reveals a rotation of the uterus of from 20 to 90 degrees. This amount of rotation is apparently corrected spontaneously before or at the time of parturition. It seems possible that some of the 180° torsions of the uterus causing dystocia at the time of parturition may have their onset at some earlier period of gestation. If circulatory embarrassment of the uterus does not develop, no symptoms of torsion will be observed until the onset of parturition when the fetus cannot be expelled due to the narrow, twisted birth canal.

In 1 in 1,000 equine pregnancies, a single fetus may develop in both horns, bicornual pregnancy, instead of the body and one horn.⁶ With this unusual type of development, the uterus and fetus must lie diagonally in the abdominal cavity, since the length of the fetus is longer than the transverse diameter of the cavity. Bicornual pregnancy in other species of domestic animals rarely occurs because of the acute angle at which the horns leave the "body" of the uterus. In the mare a bicornual

pregnancy may in rare cases become rotated ventrally so that the two horns and the fetus come to rest under the body of the uterus. At the time of parturition this condition produces a long birth passage and severe, often fatal, dystocia.

Position of the Fetus in the Uterus

In domestic animals the tubular uterus that lies more or less parallel to the long axis of the dam requires the developing fetus the last third of gestation to assume a longitudinal position in relation to the long axis of the dam. During the first half of gestation the small fetus may lie in any direction. The length of the bovine and equine fetus after 5 months of gestation is greater than the diameter of the gravid horn. The umbilicus of the fetus, in the cow and ewe opposes the lesser curvature of the uterus with the dorsum of the fetus lying against the greater curvature or dorsal surface of the uterus. This relationship of the dorsum of the fetus to the unattached portion of the horn occurs in the cow and ewe but not the mare, sow, bitch and queen. Most authors^{1,3} agree that in advanced pregnancy in the mare, sow, bitch, and queen, the fetus rests with its dorsum or dorso-lateral side against the abdominal wall and ventral portion of the uterine horn in a dorso-pubic or dorso-iliac position. This is said to account for the rolling tactics of the mare at the time of parturition. At birth the fetus of the mare, sow, queen, and bitch normally passes through the birth canal with its dorsum against the sacrum of the dam. This is brought about by a rotation of the fetus. In the mare the lack of space for fetal development in bicornual pregnancy often results in flexion of the fetal head and neck alongside the body, and because movement is thereby limited wry neck often results.

In the cow over 95 percent of the fetuses were in anterior presentation, with the cranial extremities toward the pelvis, by the seventh month of gestation.^{1,4,6} At 7 months of gestation in the mare only about 60 percent of the fetuses were in anterior presentation but by the ninth month over 99 percent were in anterior presentation. Less than 1 in 500 fetuses in foaling mares are in posterior presentation.^{3b} Late rotations of the equine fetus probably are made possible by a rotation of the amnion and fetus within the allantoic cavity.¹ In late gestation in the cow over 95 percent of the fetuses are in anterior presentation with their cephalic poles facing the cervix.^{1,10,11} During the early months of gestation, 2 through 6 and 2 through 4, in the cow and ewe, respectively, the incidence of anterior and posterior presentations is about equal. In the ewe, over 95 percent of sin-

gle fetuses are in anterior presentation after 120 days of gestation and at parturition.³ The incidence of posterior presentations in twin ovine fetuses and possibly twin bovine fetuses is significantly greater late in gestation than in single fetuses.^{4,5} Anterior presentation occurred in 55 to 75 percent of porcine and canine fetuses at parturition.^{1,1,2,3} A high incidence of posterior presentations over a 2-year period in an inbred line of Hereford cattle bred to one bull suggested an hereditary factor might condition such mal-presentations.⁷ The reason for the very high incidence of anterior presentations late in gestation and at birth in the cow and mare is not known.

Since in the cow and mare the percentage of anterior presentations is so much higher than that of posterior presentations and the incidence of dystocia or difficult birth is so much higher in posterior presentations, the latter presentation in these two species may be pathological.¹¹ Further evidence indicates that posterior presentation is abnormal.^{1,12} In posterior presentation, compression of the fetal abdomen as it enters the pelvis expands the ribs and costal arch; while in anterior presentation the fetus is wedge-shaped thus tending to dilate the birth canal during parturition and compressing the rib cage. The passage of the fetus in posterior presentation is against the direction of its hair creating more friction and resistance. Lastly, more space is required in the posterior presentation in uniparous animals to extend flexed hind limbs.

Number of Fetuses in the Uterus

Domestic animals may be divided into two groups with respect to the number of ova normally released at the time of ovulation and therefore the number of fetuses in the uterus.

Unipara, or monotocous animals such as the cow and mare, normally have one ovum released at ovulation and one fetus develop in the uterus. Occasionally twins or in exceptional instances triplets or greater numbers of fetuses may be present. This uniparous group of animals is characterized by the presence of a well-developed cervix. The placenta of the single fetus fills both horns and the body of the uterus. The weight of the fetus at the time of parturition is about 10 percent the weight of the postpartum dam.¹ In unipara the large size of the fetus and their long extremities, make dystocia due to wedging of twins in the pelvis quite common. Sheep are usually classified as unipara but the incidence of twins and triplets is so common that the term "bipara" has been suggested for this species.

Multipara or polytocous animals such as the bitch,

queen and sow, normally have 3 to 15 or more ova released at each ovulatory period and although an embryonic mortality of 20 to 40 percent commonly may occur during early gestation in these species, usually more than two fetuses are present in the uterus. In unusual cases multipara may have only one viable fetus. In general multipara have a poorly developed cervix. The placenta of each fetus is limited to a portion of the horn. The fetuses are nearly equally distributed between the horns. The fetal membranes of one fetus rarely extend through the body and into the opposite horn. The weight of each fetus at the time of parturition is only 1 to 3 percent of the postpartum weight of the dam. The small size of the fetus and its short extremities make it more bullet-shaped. Dystocia due to wedging of the fetuses in the pelvis at parturition is rare. The average numbers of fetuses usually present in the uterus of multipara are as follows: sow 6 to 12; bitch, variable between breeds, large 6 to 10, medium-sized 4 to 7, and small bitch 2 to 4; and queen 3 to 5.

Females that have never conceived or carried young are called **nullipara**. Those that have conceived and have had only one gestation period are called **primipara**. Females that have conceived two or more times and had two or more gestation periods are called **pluripara**.

Twinning and Multiple Births in Unipara

When an uniparous animal aborts or gives birth to two or more fetuses or young they are called twins, triplets, quadruplets, quintuplets, or sextuplets.

In the mare the incidence of twin births is about 0.5 to 1.5 percent.^{1,4} Double ovulation, based on slaughter specimens, occurred in 4 to 40 percent of the estrous periods of mares.^{1,6,45} Triple ovulations were very rare. Many double ovulations occurred on the same day but the time between ovulations varied from 2 to 5 days. There was a tendency for certain mares to have double ovulations. Possibly increased nutritive intake or "flushing" as in ewes may promote multiple ovulation in the mare. Double ovulation in ponies was uncommon. Although nearly all twin equine pregnancies are of the fraternal or dizygotic type rarely an identical or monozygotic twin pregnancy is observed with a single allantois chorion, two separate amnions and with both fetuses of the same sex and markings.¹³ The incidence of triplets in mares is reported as about 1 to 300,000 single births.

In 95 percent of mares with twin ovulations one or both embryos were apparently resorbed or aborted during the embryonic period.^{23b,28} The few surviving twin embryos were usually bicornual. Between 7 and 9 months

of gestation in twin pregnancies abortion is common. A report on Thoroughbreds revealed that 64.5 percent of known twin pregnancies resulted in abortion. Only 25 percent of 124 twin fetuses were viable at birth and only about one-half of these survived to two weeks of age.³³ Of 403 parturitions in 102 draft mares 13 twin pregnancies were recorded.⁵ Nine of these twin pregnancies resulted in abortion or death of the fetuses. In two twin births both twins survived and in the other two only one twin survived. In another study 14 of 17 (82 percent) of observed twin abortions occurred between 6 and 11 months of gestation.^{23b} But 7 of 24 (29 percent) of twin pregnancies resulted in the birth of live foals.

The high in-utero death rate of twins in mares is reported to be due to a competition between the twin fetuses for placental area.^{19,33} Although the chorions may fuse, anastomosis of the blood vessels does not occur. One chorion invaginates into the other. In time the smaller severely growth-retarded fetus dies due to a lack of nutrients and may rarely mummify and remain in the uterus with the normal twin until parturition. Usually when the smaller fetus dies both twins are aborted. In late gestation the expulsion of a dead twin may be accompanied by the premature birth of the larger twin. Rarely are both twins of equal size and viable at birth. (See Abortion in Mares.)

In ewes and does the incidence of twinning is greatly influenced by the nutritional status of the animal at the time of ovulation as well as the hereditary background of twins in the breed. Of nearly 60,000 sheep in Sweden of different breeds 45 percent of ewes had twins; 2.3 percent, or 1 in 50 had triplets, 0.1 percent, or 1 in 1,000 had quadruplets and 0.009 percent, or 1 in about 10,000, had quintuplets.³⁴ Under favorable conditions 60 to 70 percent of adult sheep may have twins, 25 to 30 percent triplets and 2 percent quadruplets.^{1,2} As low as 2 percent twins are reported as occurring in certain breeds and under less favorable environmental conditions. Primiparous ewes bear twins and triplets much less often than do pluriparous ewes. Finnish Landrace sheep normally produce 2 to 4 lambs per pregnancy and larger numbers are not uncommon. These have been imported into the U.S. for crossbreeding purposes.

In goats about 63.3 percent of births are of twins.¹¹ In a report from the New York State Conservation Department (1949), the northern mountainous wooded Adirondack region of the State had a deer herd producing 4 young per 100 female fawns and 93 young per 100 does. In the southern part of the State, where much more feed was available, the deer herd produced 38 young per 100 fawns and 161 young per 100 does. This clearly illustrated the effect of nutritional and environmental

conditions on the rate of reproduction of deer in the same State. Monozygotic twins in sheep are uncommon.^{2,50}

Monozygotic or identical twinning probably occurs in cats but positive evidence is lacking even when two littermates are found in the same placental sac, synchorial embryos or fetuses. Queens are commonly polyovular having 2 or more ova in a single ovisac or follicle.^{10b}

In cattle multiple births have been the subject of much study.^{5,8,9,7,27,40,48} Records on over two million births in dairy and beef cattle showed the incidence of twinning was 1.04 percent or 1:96 single births in dairy cattle, 1:87 in humans, and about 0.5 percent or 1:227 single births in beef cattle. A recent summary of many studies on twinning in cattle confirmed these earlier reports and indicated a breed difference in the incidence of twinning.⁴⁸ The frequency of multiple births in dairy cattle may be estimated as follows.⁵

Twins	1 to 96 single births
Triplets	1 to about 7,500 single births
Quadruplets	1 to about 700,000 single births
Quintuplets	1 to about 60 million single births

Thus in the U.S. about 200,000 twin calves, 2,000 triplets and 30 sets of quadruplets are born each year. From data on nearly 750,000 beef cattle the ratio of triplets was 1:106,979 and quadruplets 1:748,855 births.

Twinning is to some extent a breed characteristic.^{8,9} The incidence of twinning in about 33,000 dairy cows in the U.S. in 1957 was 2.58 percent with 8.85 percent for Brown Swiss, 3.08 percent for Holsteins, 2.8 percent for Ayrshires and 1.95 percent for Guernseys. In 1978 in over 21,000 cows the incidence (percent) of multiple births in the dairy breeds was 4.08 for Brown Swiss, 4.75 for Holsteins, 2.33 for Guernseys, 2.62 for Ayrshires and 1.83 for Jerseys.^{7,40} Thus the larger breeds have a higher incidence of twinning. Also twinning increased from 1.05 percent for Holstein heifers to 6.18 percent in cows in third and greater parities. The better fed older cows are more likely to double ovulate and maintain a twin pregnancy. The twinning rate for Holstein heifers in another study was 1.3 percent, at the second calving it was 4.4 percent and it rose thereafter to 7 percent at 10 years of age.¹⁷

A high incidence of infertility has been associated with double ovulation in cows, as in mares.⁶ In a total of over 600 bovine ovulations 13.1 percent had double ovulations but the incidence of twinning was only 1.92 percent.³⁵ Many multiple conceptions terminate early in the gestation period in embryonic death and absorption, and later in abortion or premature birth. A study reported that 90 percent of bovine twin pregnancies were bicornual and 10 percent were unicornual.¹⁸ This is probably a reflection of a higher embryonic death rate in unicornual

pregnancy after double ovulation on the same ovary since 66 percent of double ovulations should by chance occur from one ovary.

The incidence of monozygotic or identical bovine twins and dizygotic or fraternal twins to all twins was 4 to 6 percent and 93 to 95 percent, respectively.^{5,9,6,27} The incidence of monozygotic bovine twins to all like-sexed twins was 8 to 12 percent or about 10 percent. The incidence of monozygous twins to all cattle births was 0.05 to 0.3 percent. The incidence of monozygotic twins to all twins varied from 0.7 to 18 percent. Monozygotic twins arise from one fertilized ovum that divides into two zygotes in the oviduct or soon after entry into the uterus.^{42b} Dizygotic twins usually arise from the ovulation of two follicles, often one in each ovary, or rarely the rupture of a single follicle containing two ova.¹ Monozygotic twins may occur as members of triplet or greater multiple births. The higher the order of multiple births, the more likely the occurrence of monozygotic pairs.⁵ Monozygotic twins are of value in many types of nutritional, physiological and behavioral experiments in which animals with the same genetic makeup are desired for the evaluation of different environmental factors. Monozygotic twins have similar characters in respect to color, color pattern, number of teats, topline, tail, hair whorls, muzzle pattern, etc. They are always of the same sex and have the same blood type. Skin or organ grafts survive for an indefinite period when exchanges are performed between monozygotic twins.

Dizygotic or fraternal twins bear no greater resemblance to each other than do full siblings. Dizygotic twins have different blood types that frequently show blood chimerism due to early anastomosis of the placental vessels of the two twins and the exchange of primitive erythrocytic cells that become established in both embryos.^{52,53} From information based on a study of freemartinism approximately 90 to 92 percent of all bovine twins develop placental anastomoses.⁵⁷ In 21 cases studied all 9 unicornual twins developed placental anastomoses. Hemoglobin and transferrin characters in blood also showed chimerism. Thus the study of immunogenetics is of value in the diagnosis of freemartins.

Immunogenetics is the branch of genetics concerned with the inheritance of antigenic and other characters, especially blood factors, relating to the immune response. Rapid advances in this science have been made in recent years. In domestic animals the most study and progress has been made in cattle where blood typing using 80 different reagents,^{7c} about 50 routinely, has contributed significantly to the artificial insemination industry. Blood typing can usually solve problems of questionable parentage in nearly 100 percent of cattle

and 95 percent of horses by eliminating animals that are not the sire or dam of a particular individual. On the basis of 1347 parentage tests 20 percent of cows bred artificially to two different sires at 1 to 11 day intervals became pregnant on the first service while 6 percent of cows conceived on the first service when bred twice at 15 day intervals.⁴ Thus blood typing for determining parentage should be performed when a cow is bred to two different sires at an interval of 16 days or less or when the gestation length is 8 to 10 days shorter than expected on the basis of the date of the last service or when the identity of the sire is in doubt. If the sire has been blood-typed, samples from the offspring and dam when typed will invariably reveal whether the sire is, or is not, a parent of the offspring.

Immunogenetics has proven useful in the study and identification of monozygous twins and nonchimeric or chimeric dizygotic twins and freemartins by means of blood factors. It has even aided in the discovery of chimeric animals born as a single fetus where the other "twin" was lost, aborted, or mummified. In recent years electrophoretic studies of serum proteins and transferrin types in blood and the use of tissue transplants or grafts have expanded the scope of this field.^{5,6,7,8,9,10} Studies have been made to see if certain blood characters are related to other desirable or undesirable traits in cattle to aid in early selection or elimination of animals. At present there appears to be little evidence of progress in this area.

All dairy bulls used artificially and purebred stallions of a number of breeds (Thoroughbred, Morgan and others) in the United States must presently be blood-typed to facilitate the accurate determination of parentage. Blood typing in horses is practical and with the present number of reagents parentage determination was satisfactory in practically all cases.^{1a,b,c,2b,7b,c,10} The current status of blood-typing in horses, with special emphasis on the Thoroughbred horse, has been recently reviewed.^{1a,b,c,2a,b} Presently there are 16 different blood antigens and serum proteins that are available for the determination of parentage or identification. In recent years an equine lymphocyte antigen (ELA) system with 10 initial specificities has been developed similar to the HLA system in man that may be incorporated with the former tests in the future to increase the accuracy of blood-typing of horses. A number of breed registries are presently blood-typing stallions and are considering blood-typing mares and all foals. An excellent review of blood groups in the larger domestic animals was compiled in cattle, horses, sheep and pigs.^{7b,c,8}

The study of canine blood groups has indicated that most cases of hemolytic disease in newborn pups is associated with type A positive pups and A negative dams

immunized against type A blood.¹¹ With further work and the development of more reagents greater accuracy in parentage determination will be possible. More immunogenetic studies in these and other species of animals will undoubtedly be made in the future.

A developing area of immunogenetics that shows promise of being highly informative is the study of transplantation or histocompatibility antigens that are co-dominant and inherited in a Mendelian fashion.^{1a,b,c,2a,b} One group of genes that codes the strongest for these antigens is located at one point on one of the chromosomes. It is called the major histocompatibility complex or lymphocyte antigen system. Because of the extreme polymorphism of the major histocompatibility complex (MHC), it will doubtless be of use as an adjunct to current methods of parentage determination, such as red blood cell typing. It may eventually replace those systems by virtue of its greater discriminatory ability. Furthermore because MHC has been shown to control immune response genes in laboratory animals and man, there are implications for selection of resistant genes in the MHC in domestic animals in the future in areas of disease resistance, avoidance of allergic conditions and possibly in certain infertility problems.

A **freemartin** is an infertile female with a modified genital tract born cotwin, or in greater multiples, with a male with which it has exchanged whole blood.³ In a summary of reports on 348 unlike-sexed twins, 91.4 percent of the female twins were sterile and the other 8.6 percent were fertile.⁵ Thus out of 10 to 12 females cotwin to bulls only one is fertile.⁵ This infertility is of importance and interest from both the economic as well as the scientific viewpoint. The freemartin is one of two dizygotic individuals that are of different sexes and do not resemble each other. Two corpora lutea are invariably present in the ovaries. Judging from statistics on sex ratios the freemartin should be a female. There is rarely any sex intergrading between the freemartin and the male. Freemartins have been proven to be genetic females as they are positive for sex chromatin (Barr) bodies and their tissue cells have a female, XX, karyotype.^{29,42}

The development of the freemartin condition occurs when the blastodermic vesicles from each developing zygote meet and fuse in the uterus about day 18 to 20 of gestation.^{3,5} By the time the embryo is 28 days old the allantois chorion and blood vessels of the two placentas have united. This occurs well before sexual differentiation, which takes place about the 30-mm. stage or about 40 to 50 days of gestation.

Lillie (1916) originally proposed that the interstitial cells of the testes of the male developed earlier than the

female ovaries and secreted an androgen that reached the female embryo by way of the anastomosing blood vessels in the placenta and this inhibited the development of the female gonads and genital tract.³⁸ This theory has been modified by recent research to show that the H-Y antigen of the male fetus governs the development of initially indifferent gonads of the female twin toward the male mode and subsequent androgen and antimüllerian hormone produced by the gonads of the male twin and possibly the freemartin, suppress the development of the uterine tubes, uterus and cephalic portion of the vagina and promote the development of mesonephric duct remnants such as the vesicular glands^{14a, 16, 30, 43a, b, 44a, 57b} (See Chapter III on Intersexuality) (See Figures 55 and 56).

In the "pseudohermaphroditic" freemartin the "ovaries" usually fail to develop and remain small, about the size of a flattened barley grain, and undifferentiated. In rare cases some differentiation toward the female or male gonad may occur. There was no relationship between the degree of abnormality of the genital tract of the freemartin and the number of XY lymphocytes in the blood. In both the freemartin and the bull cotwin the numbers of these cells in the blood varied from less than 5 percent to more than 95 percent.^{16, 39} The vulva is fairly normal except for the occasional presence of a prominent clitoris and a large tuft of vulvar hair. In the yearling animal,

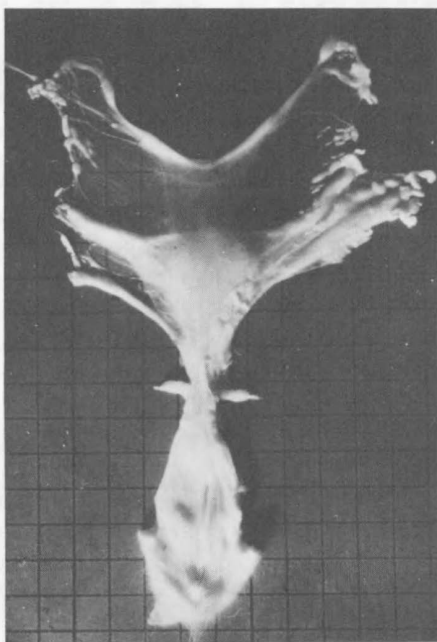


Figure 55. Freemartin genital tract. Note rudimentary uterine horns, grain-sized gonads, lack of cervix and remnants of vesicular glands (mesonephric duct structures).

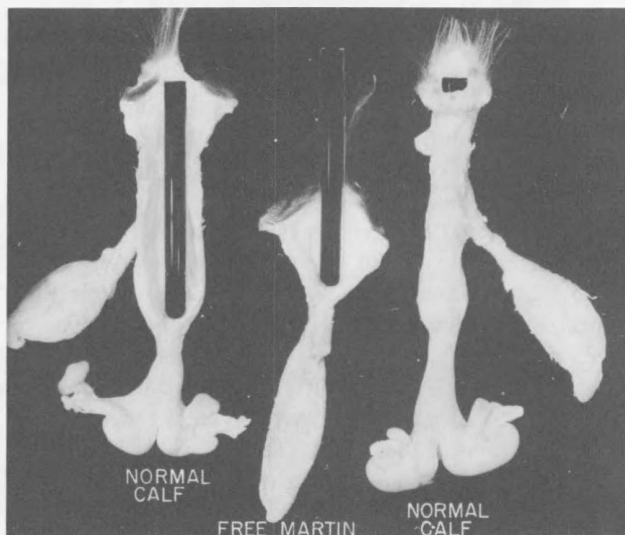


Figure 56. Clinical diagnosis of a freemartin. Note a normal vagina is lacking. (Courtesy M. G. Fincher.)

no estrous cycles occur; the udder and teats remain very small and the animal's external characteristics resemble a steer.

For a definitive diagnosis of the freemartin condition Fincher²¹ advised that a 3/8- to 1/2-inch test tube or glass speculum be inserted with lubrication into the vulva of the "heifer" in question (See Figure 56). If the animal is a freemartin the tube will insert no farther than the caudal portion of the vagina or about 7.5 to 10 cm. in a young calf, as there is no normal vagina. If the female is normal some resistance may be encountered when the test tube passes through the vulvovaginal region. But it then will pass 5 to 7 inches into a freely dilatable vagina and the use of a light will reveal a normal small cervix. In the freemartin the usual vaginal opening cannot be found anterior to the urethral opening on the floor of the vulva. A possible chance for error in this technique is in rare heifers with an imperforate hymen. After the freemartin becomes 8 to 14 months of age, a rectal examination is possible. This reveals the marked arrest in the development of the vagina, cervix, uterus, and gonads. Usually these structures cannot be found on rectal examination or they are extremely small. Pseudohermaphrodites may be mistaken for the freemartin condition. In these cases further careful in-depth diagnostic, cytologic, histocompatibility and other tests might be indicated.

In rare instances a typical freemartin may be born as a single calf. This individual was probably cotwin to a male fetus that died *in utero*, mummified and was ex-

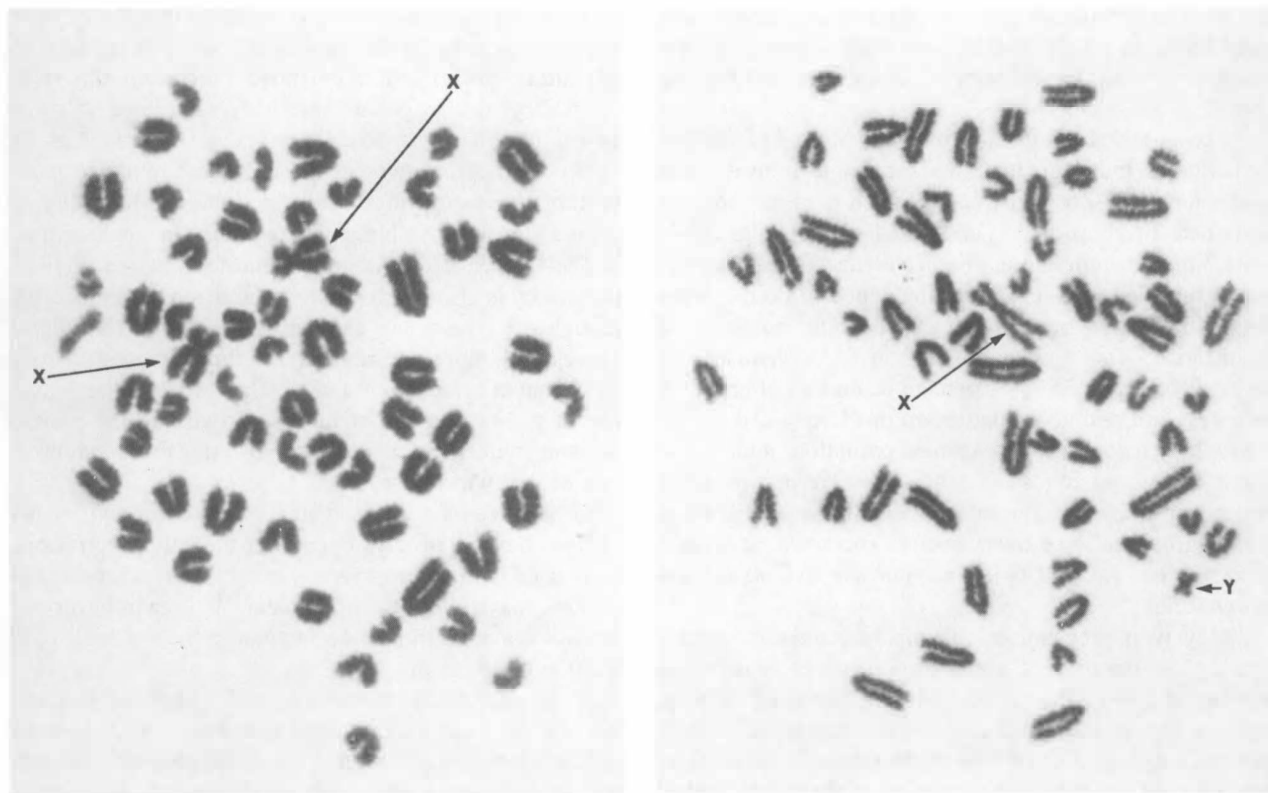


Figure 57. XX and XY white blood cells from a chimeric bull, cotwin to a freemartin. The chromosomes are in metaphase. (Courtesy of H. O. Dunn.)

pelled unobserved in the fetal membranes. Fertile, chimeric, heterosexual twin bovine females have been reported.^{43b} In these cases choriovascular anastomosis probably occurred after the differentiation of the ovaries and genital tract.

Most bovine twins are blood cell chimeras because of early placental vessel anastomosis. Of 74 pairs of heterosexual twins 89.2 percent had erythrocyte chimerism including 12 freemartins and their bull cotwins. None of the 8 females born cotwin with bulls and not having erythrocyte chimerism were freemartins.⁵¹ The percentage of heterozygous twins that would tolerate reciprocal skin grafts was the same as the incidence of freemartins indicating that the early transfer of blood elements between the fetuses caused the development of tolerance.⁴ About 90 percent of unlike-sexed twins have XX/XY white blood cell chimerism (See Figure 57).^{15,16,20}

Male chimeric cotwins to freemartins are usually considered to be fertile. However recent studies of chimeric bulls in artificial insemination studs showed that the number of XX lymphocytes in blood of these bulls varied from 5 to 95 percent. Seven of 12 chimeric bulls

(58%) were culled because of poor quality or no semen compared to less than 6 percent of 128 single-born bulls. The reasons for the poor reproductive performance in many of the chimeric bulls was speculative.^{14,15,16,49} In early cytogenetic studies a few authors reported finding XX cells in the testes of young calves.⁴⁴ Since then no such findings have been reported in male calves or mature bulls cotwin to freemartins.¹⁶ Further studies are indicated.

Freemartinism is rare in other domestic species of animals but probable cases have been reported in sheep, pigs and goats.^{1,5b,23,31,39} The chorions of twins or greater multiples in these species often fuse but anastomosis of blood vessels is apparently rare.

The Undesirable Nature of Twinning in Mares and Cows

Multiple births or twinning in the mare and cow is generally considered undesirable since it often results in an economic loss. The abortion rate of twin fetuses in

horses is exceedingly high, over 90 percent. After viable twin births in mares usually less than a quarter of the foals survive and these frequently require careful nursing care.

In cows the abortion rate for twins after 3 months of gestation is much greater than for single fetuses. It is estimated that 30 to 40 percent of such twin pregnancies terminate in abortion.^{5,17} In normal single pregnancies only 3 to 5 percent end in observable abortions. Another study revealed a 13.1 percent incidence of double ovulations in a herd but only a 1.92 percent incidence of twin births. This was potentially an 85 percent loss of twin zygotes.³⁵ A 35 to 41 percent death loss of embryos in ewes with double ovulation on one ovary and only a 22 to 26 percent loss with a single ovulation⁸ underscore the high embryonic losses associated with multiple ovulations in uniparous animals, especially in double ovulations from the same ovary even in sheep where genetic selection has favored twin and multiple ovulations and pregnancies.⁴⁸

Many twin pregnancies in unipara terminate prematurely. The duration of gestation for bovine twins is an average of 5 days shorter than for single calves.^{5,7,48} Male twins were carried 1 to 2 days longer than twins of both sexes, and 3 to 5 days longer than female twins. The incidence of abortion and premature birth is even higher in triplets and greater multiples. Fewer fertile female progeny are associated with twinning in cattle than with single births because male and freemartin calves comprise about 65 percent of twin offspring.¹⁷

Viable twins are of smaller size and vigor than single young. Single bovine males weigh 25 to 45 percent more than twin males, and single females weigh 30 to 50 percent more than twin females.^{5,7} This reduced weight of the individual twin is possibly due to a reduced amount of available nutrients for each fetus, and to the shortened gestation period. The combined weight of both twins is usually 35 to 40 percent greater than that of a single calf. A much higher percentage of dead fetuses are expelled at term in twin births than in single pregnancies. About 5 percent of twins are expelled dead at term, compared with 0.9 percent for single calves. In addition about four times as many twins die at a young age than do calves born singly.^{5,8,9,7}

Following twin births or abortions, delayed uterine involution, retained placenta, septic metritis, and temporary or permanent sterility are common. Retained placenta occurs in about 50 percent or more of twin calvings, 5 to 10 times more frequently than in single births. The placental retention is probably due in most cases to the abbreviated gestation period, to a prolonged parturition, and to a delayed involution of the uterus.¹⁷

Many authors cited evidence to show that the calving interval especially in dairy cattle, following twinning was definitely prolonged over those preceding the twin pregnancy⁹ due to greater infertility associated with retained placenta, postpartum metritis and other factors. In beef cows nursing two calves, a delayed return to postpartum estrous cycling usually occurs. The mortality in dams following twin births is higher than in single births.

The incidence of dystocia at the termination of twin pregnancy is also much greater than in single births even though the fetuses are smaller.⁷ This is due to various causes including: the atonicity of the distended uterus; the frequent presence of a dead, flaccid fetus; the wedging of the extremities of bicornual twins in the pelvis; and the frequent occurrence of posterior presentation in one of the twin fetuses.

In dairy cows decreased milk production and an increased number of days open after the calving probably associated with the postpartum metritis and other disease factors, may follow twin pregnancy.^{7,9} If twin births are not associated with disease factors, increased milk production often results.

Twins are uneconomical for herd replacements since half the pairs consist of male and female and 91 percent of these females are sterile. The male calf may be normal or have reduced fertility, but in most dairy herds these male calves are sold for veal. In beef herds this latter factor is not important. The advantages and techniques for increasing the numbers of twins have been studied in beef herds with the goal of producing more beef per cow unit.³⁷ Neither selection, hormonal induction nor embryo transplantation (inovation) have proven practical. Furthermore the behavioral response of beef cows having twins under range conditions requires further study.^{2,48}

Induction of twinning in beef cattle was accomplished by embryo transfer bilaterally, an embryo placed in each horn, and unilaterally by transfer of an embryo five days after natural service into the horn contralateral from the ovary containing the corpus luteum.^{2b} The twin pregnancy rate at 45 days of gestation was 71 and 66.6 percent and the twin calving rate was 50 and 41 percent in 35 cows and 39 heifers, respectively. The incidence of dystocia was the same, 20 percent, for the beef dams producing twins or single calves but the incidence of retained placenta was higher 14 percent and 0 percent, respectively. Calf loss was slightly higher in twin births. Thus twinning in beef cattle may have less contraindications than in dairy cattle.

For the above reasons it does not appear that selection, hormonal treatment programs, or embryo transfer procedures to promote twinning in the dairy or beef cow or

mare is presently either economically feasible or desirable.^{7,9} However, dairy cows having twins had a higher production of milk, except possibly the lactation following pathologic twin calvings, thus favoring their genetic selection by dairymen. This should result in a rise in the incidence of twinning as indicated by a rise from 2 to 3 percent to 4 to 6 percent in twinning in a short period of time in New York State.^{6b,21b}

Causes of Twinning

The causes of multiple births should be noted so that possible means to prevent this generally undesirable occurrence may be considered. The causes of twinning in uniparous animals may be divided between those which are environmental and those which are hereditary.

Environmental causes of twinning that have been reported include: **Age of the dam**—It is well known that in sheep, cattle and humans the incidence of twinning in the young is low and increases with age until senile changes commence, at which time the incidence again is lowered.^{17b} A twinning frequency of 1.3 percent for first calvings, 4.4 percent for second calvings and then a gradual rise to 7.1 percent for the tenth calvings was reported.¹⁷ Other workers^{5,7,36,48} similarly reported that in cattle there is a consistent rise in multiple births up to 5 or 6 years of age. This rise levels off and then drops after 8 to 12 years of age.

Significantly increasing the plane of nutrition; "flushing" in ewes, does and sows for several weeks prior to breeding has been shown to increase the number of ova ovulated in mature females previously kept on a maintenance or marginal level of feed intake. Such a practice in cows has not been practiced to produce an increase in twinning. However a high plane of nutrition in dairy cows has been associated with an increase in the incidence of cystic ovaries and subsequent twinning. **Sires**—The immediate influence of sires on the production of twins is limited to monozygotic twins, a small percent of the total number of twins. **Injections of gonadotrophic hormones**—Increased ovulation rates or superovulation by the injection of one or two doses of pregnant mare serum gonadotrophin (PMSG) or daily injections of purified pituitary gonadotropin (FSH and LH) starting about 10 or 12 days post estrus and removing the corpus luteum manually or preferably by the injection of prostaglandin 2 to 3 days after the first administration of a gonadotropic hormone usually results in estrus and superovulation by 15 to 17 days post estrus (See Chapter on Embryo Transfer). However because of variations in the individual cow's response to gonado-

tropins, the number of ovulations cannot be controlled.³⁷ Conception rates at 60 days where 2, 3, 4 and 5 to 6 ova were released were 55.3, 48.7, 29.2 and 25.0 percent, respectively. Low conception rates were frequently observed when superovulation was confined to a single ovary. Superovulation and conception results were unpredictable and in general not highly satisfactory. Usually only about 25 to 30 percent of treated cattle had twin or triplet births.^{24,25,26,32,37,41,54}

Although the numbers of fertilized zygotes in an animal may be greatly increased by hormonal means (superovulation) or by embryo transfer, such an increase does not result in greatly increasing the number of offspring at birth either in uniparous or multiparous animals. The uterus apparently has a mechanism whereby it can and does limit the number of embryos or fetuses that will survive beyond the first few months of gestation. Although uterine capacity varies between species and breeds, it obviously plays a role in controlling the number of offspring at birth. But since most of the limiting action occurs early in gestation while the uterus is still relatively small other limiting physiologic mechanisms apparently exist. At present these latter mechanisms are not known.^{55,56}

The hereditary basis for twinning has been reviewed,^{5,17} and has been established by records of breed differences, differences between herds, sires, and families within a breed, the repetition of multiple births in the same cow, and the effect of inbreeding on the incidence of twinning.^{5,17} **Breed differences**—The incidence of twinning in beef cattle is low which may be an indication that twinning in dairy cattle is related to the high production of milk, high nutrient intakes, and to the pituitary deficiencies associated with abnormalities of ovulation, such as cystic ovaries. In the dairy breeds the incidence of twinning is highest in Holsteins and Brown Swiss, with Guernseys intermediate, and with Ayrshires and Jerseys the lowest.^{5,8} **Differences between dams, sires and families**—A herd incidence of twinning may reach 10 to 20 percent as against the overall average of 2 to 8 percent.⁵ Dizygotic twinning is affected more by inheritance than is monozygotic twinning. In one study 2.65 percent of a bull's 377 offspring were twins; but in his daughters that produced 360 calves sired by other bulls, twins occurred 9.17 percent of the time. Thus the hereditary tendency for twinning was passed by the sire to his daughters.⁵ In a large herd of Holsteins 313 multiple births, 4.2 percent of 7387 calvings, were reported. Fourteen percent of 1905 cows produced twins at one or more calvings.¹⁷ Daughters of twinning cows had twins significantly more frequently than daughters of nontwinning cows, 17.4 percent and

13.0 percent, respectively. It was also demonstrated that the sire contributed to the twinning tendency of his daughters.¹⁷ The frequency of twinning in certain cow families has been observed by many veterinarians, farmers, and research workers. In another herd, 10 of 21 families comprising 90 percent of the dairy had no twins. The other 11 families had an incidence of twinning ranging from 2.6 to 18 percent.⁵ **The repetition of multiple births in the same cow** is principally a tendency for multiple ovulation. After the first multiple birth the frequency of succeeding multiple births was 8 to 12 percent. **Cystic ovaries**—This pathological condition, occurring usually in high-producing cows during their peak of lactation, has been associated by many workers with twinning. Although cystic ovaries are associated with high production and heavy feeding in cattle, no reports or studies have been made on the effect of a high versus a low plane of nutrition on the incidence of double ovulation in cattle. Conceptions occurring soon after recovery from cystic ovaries resulted in a high percentage of twins.^{10,12} At that time recovery was spontaneously aided by repeated removal of the cysts by manual pressure. It has been observed by the author that cows treated with luteinizing hormones and bred the following heat period did not have the high incidence of twinning noted in the former study although an increased incidence of twinning should be expected in individuals with a tendency toward ovarian cysts. Another report noted an incidence of 12.9 percent multiple ovulations in cystic parities as compared to 4.2 percent in noncystic parities.³⁶ A further study¹⁷ showed that 15 percent of cows that conceived within 75 days after treatment for cystic ovaries had twins compared to 4.9 percent of the cows conceiving 75 or more days after therapy for cystic ovaries. The condition of cystic ovaries is hereditary and bulls may transmit this tendency to their daughters.^{22,46}

In herds where selection for twinning was followed, the incidence rose to 10 to 20 percent. These facts show that twinning is definitely influenced by heredity. It might even be possible to postulate that twinning was caused by a simple recessive character with modifying genes

and environmental factors that could influence its expression.¹⁷ With the increase of artificial insemination in dairy cattle and the rise in production of milk per cow, that has been shown to be closely associated with an increased incidence of cystic ovaries, the problems arising from twinning will probably become greater. This is further complicated by the generally successful treatment of cystic ovaries with gonadotropic hormones that allow cows with this inherited tendency to produce many daughters who may also be affected. There is need for further research to see to what extent the hereditary tendency toward cystic ovaries is related to the hereditary tendency toward twinning. If twinning is a serious problem in a herd, involving 10 percent or more of the cows, an older sire with a low percentage of his daughters producing twins or a son from this bull from a family free of twins should be selected as a herd sire.

There is no evidence on the heritability of twinning in horses, although twin-prone mares are often recorded. The heritability of multiple birth in sheep was reported to be rather low,⁴⁷ except in certain breeds and their crosses such as the Finn sheep. The repeatability of twinning in ewes in another study was high and amenable to selection for improving reproductive efficiency.⁴⁸

Sex Parity

Sex parity or the sex ratio is usually expressed as the percent of male births; in older references the complete ratio of males to females was given. From a theoretical genetic basis the union of a haploid, X, ovum with either an X or Y haploid sperm cell should produce 50 percent males. Records of large numbers of animals approximate this theoretical percentage. The primary sex ratio is determined at conception. The secondary sex ratio in domestic animals expressed as percentage of males at birth is shown in Table 6.^{1,8,11} Another study provided essentially the same figures.¹⁴

On a basis of 197,936 births cited by different workers on cattle, the sex ratio of calves averaged 51.12 percent

Table 6. Secondary Sex Ratios in Domestic Animals
(percent males at birth).

Horse	49.9	Ass	48.6
Cow (<i>Bos taurus</i>)	48.6–51.5	Goat	50.1–51.3
(<i>Bos indicus</i>)	50.5–51.1	Man	50.5–51.3
Guernseys	44.4	Dog	50.4–55.9
Sheep (All)	48.3–51.0	Hybrids—Jack X Mare	44.4
Merino	46.8		
Pigs	48.5–51.9		

males with variations from 42.6 to 53.7 percent because of the low numbers of cattle in some reports.⁵ In about 200,000 bovine births in the Netherlands there were 50.6 percent male calves. Fifty-six percent of abortions were male calves and at parturition 7.9 percent of males and 4.8 percent of females were stillborn.³ A healthy beef herd of high fertility at branding time had 94,436 calves, with a sex ratio of 51.1 percent males.¹² The variations from approximately 50 percent are highly interesting but not explainable at present. The age of the dam or the sire and the season of the year had no effect on this ratio. Most workers agreed that there is a much higher percentage of males at conception in domestic animals and man than at birth.¹¹ On the basis of sex chromatin studies of human fetuses obtained at lawful abortions, sex ratios at 6, 10 and 14 weeks of gestation were 89, 68 and 58 percent males, respectively.⁹ The sex ratio of fetal calves, of 5 to 10 cm., 11 to 20 cm. and 81 to 90 cm. crown-rump length were 66, 56 and 50 percent males, respectively.⁵ In another study significantly more, ($P < .01$), male bovine fetuses were present prior to 100 days of gestation.⁷ A higher percentage of males than females are conceived, absorbed, aborted, expelled dead at term, or present in dystocia.¹¹ Of 11,527 calvings in range cattle 397 fetuses were expelled dead, 59.5 percent of these were males.⁶ This is further illustrated by sex ratios in multiple births, in which there apparently is an increased intrauterine mortality of males. The sex ratio in cattle for single births is 51.1 percent males, for twins 49.1 percent, for triplets 47.6 percent and for quadruplets and quintuplets about 45 percent. The sex ratio for premature twin births in cattle was 52.7 to 53.7 percent males.⁵

Occasionally claims are made that certain specific and intentional procedures will influence the sex ratio. One of these early claims which received wide publicity was the altering of the pH of the vagina before service. These claims are usually premature and false. With the widespread use of artificial insemination many further experiments have been conducted in efforts to separate the Y-bearing spermatozoa from the X-bearing spermatozoa by electrophoresis, centrifugation, sedimentation and other techniques.^{4,10} It is known that the amount of DNA in the Y-bearing sperm cell is less than that in the X-bearing cell. These experiments have not been successful. There is no basis that beliefs such as prolonged storage of semen, breeding at certain times during estrum, using young or old males, age of cow or season of breeding, and others have any effect on the sex ratio.^{2,8} Since physical and chemical techniques were unsuccessful in manipulating the sex ratio possible genetic variations in sex ratios was reviewed.¹⁰ Evidence for a hereditary basis for alterations in the sex ratio of domestic animals

was not found. A study of XX/XY chimeric bulls cotwin to freemartins did not reveal any bulls that sired a significant excess of female calves, although a few bulls cotwin to a freemartin produced an excess of female calves in a limited number of breedings (See Dunn et al. (1979) under Freemartins). The number of animals used in an experiment to alter the sex ratio should be considered; this number should be very large for the substantiation of any such claim.

The Bacterial Flora of the Pregnant Uterus

Although the literature reveals an apparent controversy on this subject, practically all workers agreed that from 20 to 80 percent of pregnant bovine uteri have some bacteria between portions of the maternal and fetal placentas, in the uterine cavity or in the organs of the fetus.^{12,12} Many pregnant uteri are bacteriologically negative. Although this may be ideal, it apparently is not essential for a healthy normal gestation and parturition. A careful examination of almost all placentas will show a few areas where some pathology or disease process, either acute and active or chronic and inactive, is present. The organisms most commonly found are streptococci, staphylococci, and coliform bacilli. Many other bacteria, molds, and viruses have been reported. These organisms gain access to the uterine cavity and placenta by way of the cervix and the caudal portions of the genital tract at the time of estrum and service, are still present from the time of a previous parturition, or they may come from the blood stream of the dam and localize in the uterus. During most of the gestation period in domestic animals, the uterus and uterine endometrium is under the influence of progesterone from the corpus luteum or placenta. During the estrual cycle the uterus of the cow is resistant to infections at the time of estrum when under the influence of estrogens, and more susceptible to infection during the rest of the cycle when the uterus and endometrium are under the influence of progesterone.^{2,13} It is possible that the favorable environment produced by progesterone, necessary to maintain pregnancy in domestic animals, may favor the establishment of infections in the gravid uterus.

The above findings may indicate to some that the presence of bacteria is of itself dangerous or harmful to the pregnancy. This is not necessarily true. One might liken the condition to an internal parasitism where a few parasites, particularly nonpathogenic parasites have no effect on the individual. It is only when the individual's resistance is overcome or an excessive number of virulent "parasites" are present that the condition reaches

disease proportions with definite symptoms and extensive pathology. It is difficult to delineate between health and disease. Slight to definite infection and evidence of disease of the placenta may be present in an apparently physiological birth. In the more severe infections greater damage to the placenta and endometrium may produce fetal deaths, maceration of the fetus, abortions, premature births, dystocia, retained placentas, septic metritis, and subsequent sterility. These latter diseases may be associated with the lowering or lack of resistance of the dam or the fetus; previously undiagnosed damage to the endometrium; and the type, pathogenicity, virulence and numbers of organisms present during the various stages of gestation.

Although healthy, gravid uteri frequently have some bacteria present, the healthy, nongravid uteri does not have a bacterial flora. Most workers, find healthy non-gravid bovine uteri free of bacteria.¹² Judging from extensive work based on cervical and uterine cultures made during estrus, this is true in the normal healthy mare. A number of other workers have reported that infertile cows, or cows that have an obvious genital disease and have failed to conceive often may have infection and endometritis of a sufficient degree to prevent conception.^{4,12}

DURATION OF GESTATION

Many factors influence the duration of gestation. The length of the gestation period differs between the animal species, breeds and hybrids (See Table 7). In cows and mares male fetuses are carried one to three days longer than female fetuses.^{23,30} Male fetuses in cattle also weigh 2 to 10 lbs. more than female fetuses. Young cows in their first and second gestation periods carry fetuses one to two days less than older cows. It appears that calves born during the winter or spring have slightly longer gestation periods. Foals born from January through April have gestation periods about 5 to 10 days longer than foals born from May through September. When mares were exposed to 16 hours of daylight through the last half (December through April) of their gestation period, the length of gestation was reduced 10 days over control mares, 338 vs 348 days. This prolonged exposure to extended light had no effect on the fetus, foal size, hormonal levels or the postpartum period to ovulation.^{30b} Differences in gestation length between years may be as great as 6 to 7 days.^{30a} In rare instances, mares will have gestation periods up to 375 days in length, and even up to 400 days with a live foal being produced.^{30,33,41,50} Most studies indicated that the breed of the sire and dam has

an influence on gestation length in cattle, sheep, horses, hybrids and pigs (See Table 7).^{4,5,6,14,30,31,46,49} The length of gestation is primarily a characteristic of the fetus and that by selection of male and female calves having a short gestation period the mean length of gestation could probably be decreased 10 days within three generations.¹⁴ Thus each individual fetus determines its own length of gestation.

In 290 normal pregnancies in Beagle bitches the mean gestation length was 65.3 days, range 57 to 72 days.^{12b} In 54 of 62 cycles in which the LH peak was accurately determined by radioimmunoassay and pregnancy occurred, the apparent gestation lengths ranged from 58 to 71 days with an average of 64.7 days. The interval from LH peak to parturition was less variable, 64 to 66 days, average 65.1 days. The first acceptance of the male for mating by the bitch usually occurs two or three days after the LH peak so this further confirms the 62 to 63 day mean normally given as the duration of gestation in the bitch.

Short gestation periods are often associated with abortions and premature births. The gestation period of twin fetuses in cattle is an average of 3 to 6 days shorter than gestation periods of single fetuses.³¹ In beef cows with multiple pregnancies following the administration of PMSG, the duration of pregnancy for single fetuses, twins, triplets, quadruplets and quintuplets was 280.8, 277.4, 269.2, 262.5 and 258.0 days, respectively.⁵⁸ A similar, but more moderate, reduction in the length of gestation has been observed in ewes and does carrying two or more fetuses.⁴⁶ Adverse disease factors influencing the health of the endometrium and placenta or infecting the fetus may cause abortion or short gestation periods. Besides infections these adverse influences may also include malnutrition, chronic debilitating diseases, deficiency diseases, starvation, severe stress or other conditions favoring or causing abortion or premature birth. Premature births in cows are those between 250 and 270 days of gestation, in the mare between 310 to 330 days, in sows between 105 and 110 days, in ewes between 130 and 140 days, and in bitches and queens between 52 to 58 days. Special care and supportive therapy is often necessary for these premature neonates if they are to survive and even then early deaths are common. A genetic involution of the corpus luteum of pregnancy associated with hyperplastic adrenal cortices resulted in abortion in inbred Angora goats.⁶⁰

Prolonged gestation periods are observed in a variety of conditions in animals³⁴ including:

- (1) Iodine deficiency in sows, or the administration of thiouracil to produce hypothyroidism, caused gestation periods 4 to 10 days longer than normal

Table 7. Duration of Pregnancy in Domestic Animals.*

Days			
Cow—273 to 296			
Aberdeen Angus	273 to 282		
Ayrshire	277 to 279		
Jersey	277 to 280		
Holstein	278 to 282		
Shorthorn	281 to 283		
Guernsey	282 to 285		
Hereford	283 to 286		
Brown Swiss	288 to 291		
Brahman	292 (Range 271–310) ⁴⁷		
Afrikaner	293 to 296		
Horse—327 to 357			
Light breeds	340 to 342 (Average) ^{21,30,48}		
Draft breeds	330 to 340 (Average)		
Stallion X Ass	350 (Hinny) ³¹		
Jack X Mare	355 (Mule) ³¹		
Ass	365 to 375		
Sheep—140 to 155			
Coarse or Medium Wool Breeds	140–148		
Southdown	143 to 145		
Dorset	144		
Hampshire	145		
Shropshire	146		
Corriedale	149		
Finnish Landrace	145		
Fine Wool Breeds			
Rambouillet	150		
Merino	150 (147–155)		
Targhee	150		
Swine	111 to 116		
Dog	60 to 63 (57–70)		
Cat	56 to 65		
Siamese cat	63 to 69		
Goat	148 to 156		
Other Animals	Days	Other Animals	Days
Chinchilla	111 to 128	Coyote	60 to 68
Guinea pig	63 to 70	Deer	200 to 210
Hamster	16 to 19	Elephant, Indian	615 to 650
Mouse	18 to 20	Fox	51 to 52
Rabbit	30 to 32	Kangaroo	38 to 40
Rat	22 to 23	Lion	105 to 112
Bear	208 to 240	Woodchuck	28 to 32
Bison	270 to 276	Mink	42 to 53
Egyptian buffalo	316 to 318	Opossum	7 to 13
Camel, Bactrian	333 to 430	Raccoon	63
Dromedary	315 to 350	Rhinoceros	530 to 548
Man	271 to 289	Tiger	105 to 113
Squirrel	28 to 40	Wolf	63

*The above data from various sources, including^{2,4,7,2,4,12b,18a,21,23,30,31,35b,41,46,48a,b}

with poorly viable, goiterous, hairless pigs.

- (2) Delayed parturition in sows, bitches, ewes and cows has been produced with large continued injections of progesterone or progestins. Most fetuses died in the month following a normal length of gestation and became macerated or mummified.^{8,36}
- (3) Ewes consuming *Veratrum californicum* about the 14th day of gestation, causing severe deformities of the face and head with hypoplasia or aplasia of the hypophysis, had greatly prolonged gestation periods of up to 230 days with fetal giantism and rupture of the prepubic tendon. Prolonged bovine gestation periods were associated with the ingestion of *Veratrum album* in Japan. The defective bovine fetuses were shortlimbed, semi-hairless and had an aplasia of the hypophysis.^{34b} Prolonged gestation in Karakul sheep in South Africa associated with giant fetuses has been described but the cause, possibly genetic in nature, is unknown.¹⁵
- (4) An inbred line of sows carried their fetuses 3 to 4 weeks overtime.¹⁰
- (5) Decapitation of fetuses during pregnancy resulted in overtime small, weak edematous fetuses with adrenals one-fourth to one-fifth normal size.^{11,38,57}
- (6) Destruction of the pituitary glands of fetuses by electrocautery at 90 to 142 days of gestation produced prolonged gestations.³⁹
- (7) In a number of cattle breeds three types of prolonged gestations have been observed:
 - (a) Prolonged gestation was seen associated with postmature, long-haired fetal giants in Holsteins and Ayrshires,⁶⁴ and in other breeds in which a homozygous recessive autosomal gene was involved. These postmature fetuses had long hooves; their incisor teeth were erupted and dehydration was evident. These calves had hypoplastic adrenals.^{17,31} In this condition the gestation was prolonged for 20 to 90 or more days and the fetuses weighed from 130 to 200 lbs. Vaginal delivery was impossible and severe dystocia resulted unless a cesarean operation was performed early. Affected calves had hypoglycemia and died shortly after delivery with an Addisonian-like syndrome characterized by marked adrenal insufficiency and possible anterior pituitary gland abnormalities. Following birth by caesarean section a continuous regimen of corticosteroids was necessary to maintain the life of the calf.
 - (b) Prolonged gestation is also seen associated with cretin-like, immature fetuses with cranial and

central nervous system anomalies, including hydrocephalus, anencephaly, or cyclopia and short, deformed loose-jointed legs with an aplasia of the anterior pituitary gland and a degree of hairlessness. The adrenal glands may be very hypoplastic or absent. These defective fetuses may be carried 20 to over 230 days overtime, average 120 days, and they are relatively small in size. Hydramnios is frequently present. If parturition commences dystocia may occur but is not a serious problem. It is seen most frequently in Guernseys, Swedish Red and White cattle and possibly Ayrshires. This anomaly is due to an autosomal recessive mode of inheritance.³⁵ (See Figure 33.)

- (c) The author has observed 4 Holstein calves with cerebral hernia, "catlin mark," a sloping forehead, a greatly reduced cranial cavity and abnormal brain, long hooves and hair, dystocia due to its excessive size after a prolonged gestation, 20 to 60 days overtime, and death before or soon after birth. (See Figure 29.) In one of these calves that was autopsied the adrenals were markedly hypoplastic. In a similar case⁹ the cerebellum was absent, the cerebrum was small and the pituitary gland was absent on gross examination, the calf weighed 130 pounds and was delivered by caesarean section on the 329th day of gestation.

In these last three conditions no prepartum or partum changes were observed at the time of expected parturition and the udder was undeveloped until after the fetus had been removed. Parturition does not occur unless the fetus dies *in utero*. As pointed out, no bonafide greatly prolonged gestation in a cow has ever produced a morphological or metabolically normal calf.³¹ Prolonged bovine gestations including endocrine levels in the dam and fetus were reviewed recently.^{16b}

In a recent study bilateral adrenalectomies on ovine fetuses were performed at 110 to 120 days of gestation. This resulted in prolonged gestations of 157 to 180 days. When only one of a pair of twin fetuses was operated on the normal intact fetus died *in utero* while the adrenalectomized fetus survived the prolonged gestation period but died at or soon after birth. Thus there is a good correlation between prolonged gestation in cows and ewes and abnormal anterior pituitary glands and adrenal cortices. Aplastic, hypoplastic or damaged pituitary glands of the fetus result in prolonged gestation. Hyperplasia of the adrenal gland with excess glucocorticoid production results in abbreviated gestation in goats.⁶⁰

Aplasia or severe hypoplasia of the adrenal gland, secondary to a pituitary deficiency, results in prolonged gestation in cattle. The control the fetus exerts through its pituitary-adrenal axis over the duration of gestation is obvious. This control is probably triggered by the release of ACTH from the fetal pituitary gland.³⁹

Premature birth of viable young can occur in the cow from about 240 to 270 days and in the mare from 310 to 320 days. Delayed births in cows are usually considered as gestation periods over 295 days, except for Brown Swiss and Brahman cattle, and in mares over 350 days. These figures are relative but are given because viable, apparently normal young may be produced, the parturitions be uneventful and the dams survive, over a wide range of gestation lengths.

The birth weight of newborn animals is closely associated with gestation length and other factors acting during the gestation period. In this area studies in cattle have predominated. The average birth weight of calves for the various breeds are as follows: Sindhi, 45 lbs; Jersey, 55 lbs; Aberdeen Angus, 60 lbs; Guernsey, 68 lbs; Africander, 71 lbs; Hereford, 72 lbs; Shorthorn, 72 lbs; Ayrshire, 73 lbs; Holstein, 92 lbs; South Devon, 100 lbs; Brown Swiss, 101 lbs. and Charolais, 105 lbs.⁴ Calves born to mature cows are heavier than calves from heifers. There is a positive correlation between the weight of the dam and sire and the calf. Season of the year at birth had little influence on the weight. Bull calves were generally 2 to 9 lbs. heavier than female calves. Most authors indicated the sire had a significant effect on the calf's birthweight. In general the longer a fetus was carried the greater the birth weight. Birth weight and gestation length are influenced by heredity and influenced more by the calf than the dam that carries the calf except possibly where breeds of great disparity in size are interbred. Single lambs at birth weigh about 7.5 percent of the combined weight of the dam and sire divided by 2. Individual twin lambs weighed 16 percent less than single lambs but their combined weight was 67 percent more than singles. The sire had little effect on the birthweight of lambs.⁵⁵ Boar pigs weighed 5 percent more than gilts at birth. This greater weight of male fetuses in domestic animals is probably a cause of dystocia in small primiparus females.

Hormonal Control of Gestation

The placenta connecting the fetus and mother provides best for the needs of viviparity.³ Because it is able to provide this protection, the mammal relies less on large numbers of eggs released and more on the survival of a

few young in order to perpetuate the species. During evolution the placenta has developed endocrine functions that allow a longer gestation period with the birth of young which are more mature and thus better able to cope with the external environment. In marsupials the gestation period is equal to the length of the estrous cycle, and removal of the ovary any time during pregnancy terminates the pregnancy. In the higher mammals such as the horse and primates the placenta tends to assume some of the endocrine control of pregnancy. Nervous control of the uterus is not essential during gestation in man and other animals. Conception, gestation, and possibly normal parturition can occur with complete paralysis and lack of nerves in the lower portion of the body. Gestation and the onset of parturition are entirely under hormonal control.

In the mare the fertilized ova pass into the uterus about six days after ovulation while unfertilized ova are retained and degenerate in the oviduct. This probably constitutes the earliest maternal recognition of pregnancy in domestic animals.

At approximately 12 days in the ewe, 13 days in gilts, 14 to 16 days in mares and 15 to 17 days in cows after estrum and fertile coitus, the trophoblast or blastocyst has grown very rapidly and brings about the maternal recognition of pregnancy. This is accomplished by the luteotropic secretions of the blastocyst that cause a persistence of the corpus luteum, a suppression of the uterine luteolysin or prostaglandin, and a cessation of the estrous cycle. The luteotropic substance produced by the blastocyst in the cow is composed of one or more heat labile molecules. In the pig estradiol, and in the mare estradiol and androgen, appear to be the major luteotropins produced by the blastocyst. However estradiol therapy will not stimulate progesterone production in bovine luteal cells.^{7,22,29}

In bitches and queens this early provision for promoting the attachment of the developing embryos is pseudopregnancy. In bitches which ovulate spontaneously, the corpora lutea that develop after every estrous period persist for about 60 days or the duration of gestation. In the queen, which requires mating or a similar stimulus to produce ovulation, the cause of pseudopregnancy is also ovulation and corpora lutea formation. The length of pseudopregnancy in the queen is about 40 to 50 days.⁶¹ The levels of progesterone in the feline blood plasma rise rapidly within 10 days of ovulation due to the formation of corpora lutea stimulated by the release of luteinizing hormone (LH) after coitus resulting in ovulation.

During pregnancy the progesterone from the corpus luteum or the fetal placenta is essential for endometrial

gland growth and secretion of uterine milk, for endometrial growth and attachment of the placenta for the later nourishment of the fetus, and for inhibiting uterine motility to aid in placental attachment. A certain amount of ovarian or placental estrogen appears necessary to enhance the effect of progesterone and in later pregnancy to produce udder development, relaxation of the pelvic ligaments, initial uterine tonus, cervical relaxation and to sensitize the uterus to oxytocin and prostaglandins. Other hormones essential in maintaining pregnancy are the gonadotropic or luteotropic hormones from the anterior pituitary gland necessary for the persistence of the corpus luteum and its active secretion of progesterone. In the mare gonadotropins (PMSG or ECG) are produced by the endometrial cups and in woman by the chorion (HCG) of the fetal placenta during the first trimester of pregnancy. Further studies are needed to fully explain the role of PMSG in the maintenance of pregnancy. It is also obvious, as noted in the previous section on prolonged gestation, that the endocrine glands of the fetus, thyroid, adrenals, gonads, anterior pituitary gland and possibly others besides the fetal placenta, play important roles in maintaining and terminating pregnancy. Further study is necessary to determine the exact interplay between maternal and fetal hormones in maintaining pregnancy in the various species of animals.

In the cow, doe, sow and bitch the corpus luteum of pregnancy is required throughout gestation to maintain a normal gestation period and permit a normal parturition. Removal of the corpora lutea or ovariectomy before term in these animals results in abortion or premature birth.^{4,18,20,27,54} The weight of single bovine corpora lutea throughout pregnancy was 6.4 gms (5.5 to 8.5 gms) and each of twin corpora lutea was 3.9 gms.⁶³ The ovaries or corpora lutea may be removed in the queen after 50 days, the mare after 70 to 150 days and the ewe after 55 days of gestation and pregnancy will continue normally and without interruption.^{4,6,32} In the latter animals the placenta and fetus produce the necessary steroid hormones, progestins and estrogens to maintain pregnancy. Pregnancy may be maintained in most cows ovariectomized during pregnancy by the injection of 100 mg of progesterone daily, 500 to 1000 mg. of Repositol progesterone every 7 to 10 days, or feeding 4 mgm MGA (melengestrol acetate) daily.^{10,63} In sheep the placenta or fetal cotyledons were the major source of progesterone the last 100 days of gestation since removal of ovaries from ewes after 50 days of gestation did not cause abortion or a drop in the blood serum level of progesterin.^{37,44}

Cole and Cupps and others^{4,6,62} have summarized in graph form the blood levels of progesterone and estrogen

in the larger domestic animals during the gestation period:

The cow has progesterone levels of 6 to 10 ng/ml from the development of the mature corpus luteum to within a day of calving. The estrogen levels are low the first 4 months of pregnancy, reach a level of about 100 pg/ml between 140 and 245 days and then rise precipitously to a peak of 1500 to 10,000 pg/ml two to five days before parturition. Both corticosteroids and prolactin levels rise rapidly from base levels the last 24 to 48 hours of gestation.

The ewe has progesterone levels of 2 to 3 ng/ml at 50 days, a rise to 12 to 20, or more, ng/ml at 125–130 days, then a steep fall to less than 1 ng/ml at lambing. Estrogens during gestation are low, 50 pg/ml and rise to 100 to 400 pg/ml a day before parturition. Both corticosteroid and prolactin levels rise rapidly the last few days of gestation.

The sow has progesterone levels that rise rapidly to a peak of 35 ng/ml on day 12 decline to about 17 ng/ml at 24 days and then remain nearly stable until a fall to less than 1 ng/ml at parturition. Estrogens are about 20 pg/ml for 24 days and then rise to 100 pg/ml by 90 days and rise precipitously to 300 pg/ml the last 10 days of gestation.

The doe has progesterone levels that rise from 5 ng/ml to 33 ng/ml by 90 days and then decline to 7 ng/ml at 140 days and to very low levels by parturition. Estrogen levels are low, 5 pg/ml until 30 days, rise steadily to 15 pg/ml at 50 days, 272 pg/ml at 85 days, 450 pg/ml at 125 days and 622 pg/ml at parturition. Prolactin levels rise rapidly the last few days of gestation.

The mare has progesterone levels that rise to 7.5 ng/ml at 8 days, and plateau at 10 to 15 ng/ml from 50 to 120 days and decline to 5–7 ng/ml at 150 days and 2 ng/ml at 180 days and remain low the remainder of gestation. However certain progestogens including the 5 α -pregnanes, increase to 8 to 16 ng/ml from 180 days to the end of gestation.^{24,40,43,48b} These latter progestogens apparently are produced by the placenta. Progestogen blood level in mares is quite high at parturition but drops rapidly within 24 hours after parturition. This pattern differs from other domestic animals but not the woman. Estrogen levels in the mare are 10 to 20 pg/ml until day 80 when they rise gradually to a peak of 825 pg/ml at 210 days then fall gradually to 370 pg/ml on day 300 and 150 pg/ml near parturition after which estrogen levels fell rapidly. It is interesting to note that the greatest size (7 × 4 cm.)

of the fetal gonads nearly coincides with the peak blood levels of estrogens at 180 to 240 days of gestation. Equine fetal gonads have massive numbers and size of interstitial cells. Fetal gonadectomy at 210 days resulted in a marked reduction of conjugated and unconjugated estrogen levels in the maternal blood. Progesterone levels remained unchanged.⁴⁵

Equine gonadotropin, PMSG or ECG produced by the endometrial cups rises rapidly from 0 IU/ml at 36 days to a peak of 67 IU/ml at day 57 then declines to less than 1 IU/ml by day 150. Ponies have higher levels up to peak values of 400 IU/ml, while mule pregnancies have very low levels of PMSG. Since the endometrial cups are of fetal cell origin, their degeneration and involution at 120 to 150 days of gestation is possibly similar to the rejection of a heterologous tissue graft.^{1b} The high levels of PMSG in mares have little effect on the ovaries. However, ovulation and the formation of secondary or accessory corpora lutea commonly occur between 40 and 90 days of pregnancy in mares and regress by 150 days of gestation coinciding with the production of PMSG by the endometrial cups.⁴ The mare's ovaries are apparently refractory to exogenous and endogenous PMSG because the latter binds very poorly, less than 10 percent, to LH receptors and not at all to FSH receptors in the ovaries. Therefore ovulation and the formation of secondary corpora lutea occurring during early pregnancy are probably due to seasonal release of maternal pituitary FSH. PMSG may be the stimulatory factor causing the great growth of the fetal gonads between the third and sixth month of pregnancy.⁵⁶ HCG injections induced pregnancy loss when given before gestation day 38 but injections after that day did not induce luteolysis and pregnancy loss possibly because of the presence of PMSG.^{1c} Evidence has been presented that human chorionic gonadotropin, HCG, is probably a trophoblastic surface antigen that blocks the action of maternal lymphocytes and prevents the rejection of trophoblastic placental tissue during nidation of the embryo.^{1a} A similar action for PMSG in the mare seems logical since the highest levels of PMSG coincide with the period of the implantation of the equine blastocyst. The role of PMSG in the production of accessory or secondary corpora lutea for the maintenance of pregnancy is in doubt.

If an equine pregnancy fails spontaneously or is induced after the endometrial cups have formed, the cups will continue to produce PMSG until about 120 days after conception. During this period mares usually will not cycle normally or conceive due to a period of anestrus characterized by small, hard inactive ovaries, especially

in Thoroughbreds, or irregular cycles with follicular activity but failure of ovulation and infertility, especially in ponies.^{1c,d}

Corticosteroid levels in the blood of mares rose at the end of gestation as in the other animals.^{12c} Prolactin levels during gestation were variable without a definite pattern.⁴⁰

The bitch has progesterone levels that rise from 0.5 pg/ml in proestrus to 25 to 30 ng/ml at 10 days and to a peak of 40 to 50 ng/ml at 20 to 25 days of gestation. In unmated or sterile bitches, progesterone levels declined after 20 to 30 days from levels of 25 to 30 ng to less than 0.5 ng/ml after 80 days. In pregnant bitches progesterone levels declined gradually from the peak at 25 days to near parturition. Progesterone levels declined rapidly from 6 to less than 2 ng/ml the last 24 to 48 hours before whelping. Progesterone synthesis by the canine placenta is minimal. Estrogen blood levels rose gradually from about 10 pg/ml early in pregnancy to a peak of about 15 pg/ml at 50 days and then declined to 8 pg/ml at parturition. Plasma corticoid levels increased to 15 to 35 ng/ml the last few days of gestation. Prolactin increased during pregnancy with a sharp rise just prior to whelping.^{4,12,51} Twice daily rectal temperatures taken during the last week of gestation revealed a characteristic drop of 0.8 to 1.0° C (1 to 1.8° F) during the last 24 hours before whelping.¹² An interesting observation that hematocrit values in pregnant bitches fell gradually during gestation from 50 to 30 with a significant decline after days 22 to 24. This low hematocrit value at term was over 30 percent lower than that in "pseudopregnant" or nonpregnant bitches 60 days after ovulation.¹²

The queen has progesterone blood levels that rise gradually to a peak of 35 ng/ml by day 21, decline gradually to 10 ng/ml at day 60, to 5 ng/ml just before parturition and to 1 ng/ml just after parturition. In pseudopregnant or sterile queens, progesterone blood levels rise to a peak of 24 ng/ml at day 21 postovulation and decline gradually to 4 ng/ml by day 40, to 2 ng/ml by day 50 and to 1 ng/ml by days 63 to 65. The feline placenta produces significant amounts of progesterone late in pregnancy. Estrogen and progesterone profiles and levels in pregnant queens are nearly the same as in bitches. Estrogen blood levels in pregnant queens are from 6 to 12 pg/ml and rise moderately near term and drop precipitously at parturition.^{51,61}

The hormonal and other factors initiating the onset of

parturition at the prescribed time for the various species of animals involves a fairly rapid series of hormonal changes in progesterone, estrogen, oxytocin, cortisol and prostaglandin levels which will be described subsequently.

Duration of Reproductive Ability

The duration of reproductive ability in domestic animals depends basically on two factors. **First**, the breeding or reproductive life of an animal ceases when at any age physical decrepitude occurs. This may be caused by disease or by defective nutrition secondary to a loss of teeth resulting in senility and emaciation. **Second**, reproduction ceases when the reproductive organs are injured severely or their function destroyed by disease factors. In the female those diseases limiting reproduction affect mainly the endometrium and epithelium lining the tubular genital organs and less often the ovaries. In the male, pathological changes in the seminiferous tubules of the testes caused by diseases, trauma, or senile changes, are the most common causes for loss of reproductive ability. Occasionally sires may develop arthritic joints or spinal lesions that make copulation impossible and thus their natural reproductive life is terminated.

The average duration of reproductive life in the dairy cow is about 8 to 10 years of age, with the production of about four to six viable calves. In beef cattle this average duration of reproductive life may be slightly longer, 10 to 12 years. Exceptions to these averages are numerous. Cows have been recorded^{11, 15} that had calves regularly to 16 to 18 years of age and in rare cases to 25 or more years of age. Bulls usually can breed until 10 to 14 years of age and in exceptional cases up to 18 years of age.

The average duration of reproductive life in the mare is approximately 18 to 22 years. The number of mares that become pregnant and carry a foal after 24 years of age is low although a few mares were reported to have had foals from 25 to 33 years of age. In ewes and does the average duration of reproductive life is about 6 to 10 years of age but ewes and does have been known to reproduce until 16 to 20 years of age.¹² The sow is capable of reproducing until 6 to 8 years of age and occasionally to 10 or even 15 years of age. In sows the size of the litter tends to decrease after 4 to 5 years of age. Beyond this time, although the female may be capable of reproduction, the litters produced are so small that it is uneconomical to continue breeding the sow. In bitches and queens the average duration of reproductive life is about 8 to 12 years of age. However, they have been known

to produce young at 14 to 17 years of age.

Animals prevented from breeding after puberty have increased difficulty to conceive the longer the nonpregnant state is maintained. Mares that do not have foals before 10 to 12 years of age experience difficulty in conceiving after that time even though their physical condition may be excellent. Cattle not bred until 4 to 5 years of age are also difficult to impregnate and frequently develop cystic ovaries and endometrial abnormalities.⁵ Bitches that are not bred by 4 to 6 years of age frequently develop cystic endometrial hyperplasia associated with infertility and often endometritis and pyometra. Probably in other domestic species delaying conception for a long period after puberty probably has a depressing effect on reproductive ability by the adverse effects on the endometrium.

In women changes resulting in the menopause take place at an average age of 49 years.⁶ In animals, with the possible exception of the mule, this condition characterized by a nearly complete loss of oocytes from the ovaries and cessation of the estrous cycle, has not been observed. Domestic animals usually die or are disposed of for other reasons before this stage of life. Observations in animals tend to indicate that cessation of reproduction in females with little or no genital disease is a more gradual process than it is in humans. It is rather closely linked with the lack of nutrition caused by the wearing out of the teeth and the resulting senile changes produced. It has been proven in practice that if genital and mammary disease could be controlled many cows could have 2 or 3 or more additional years of reproductive life. This would be of great economic value to the farmer.

Rate of Reproduction in Animals

The rate of reproduction depends basically on three factors: the length or duration of reproductive life, the number of young produced at each parturition, and the frequency of parturition.

The first factor has been discussed. The second factor is largely a characteristic of the species of animals concerned, whether unipara or multipara. However, the number of young produced at each parturition in any species may be increased or decreased to a limited extent by hereditary factors and selective breeding. Environmental factors apparently play a minor role in most animals, but in ewes, does, deer and possibly sows a high level of nutrition during the breeding season favors a greatly increased incidence of twins, triplets and greater litter size. In multiparous animals such as the sow the size of the litter tends to increase slightly up to maturity

and then decrease in size with advancing age. A high level of nutrition prior to breeding and a lower level thereafter increases the number of porcine ova ovulated and reduces the embryonic death rate in swine, respectively.

The third factor in the rate of reproduction, namely the frequency of parturition, is of great concern to the farmer as well as to the veterinarian, since any delay in getting farm animals to conceive is of economic importance. Once conception has occurred the duration of gestation is definitely established for each species. In an ideal breeding program most cattle or horse breeders strive for a calf or foal every 12 months. Although this can be attained with certain individual animals, it is a difficult goal to reach on a herd basis.

Because of the photoperiodic breeding season in ewes and the variation between breeds, it is possible by intensive management for ewes to have three lambings in two years. Sows are regularly managed to have two to three litters of pigs per year. Many adverse management, hereditary, and disease factors are present to prevent the achievement of these goals. It requires the close cooperation and active interest of both the farmer and the veterinarian, especially in dairy cattle and horses, if these adverse factors are to be kept at a minimum. The greatest departure from the ideal breeding performance is seen in those breeds most artificially maintained, that is, the dairy cow, the race horse, and the breeds of pet dogs.¹² The adverse management, hereditary, and disease factors that tend to produce infertility, cause abortion, or result in dystocia and postpartum disease, are being studied intensively by veterinarians and animal husbandrymen in an effort to curb or control the economic waste they produce.

Abnormalities of Fertilization and the Gestation Period

Wandering of the embryo—In uniparous animals such as the cow the corpus luteum of pregnancy is rarely found in one ovary and the embryo or fetus located in the opposite or contralateral horn. The incidence of this occurrence in the cow is less than 1 percent.^{2,13} However, transuterine migration of the zygote very early in gestation is common in the mare, ewe, sow, bitch and queen. Transperitoneal migration of the ovum has not been described in the domestic animals. In sows when fertile ova were surgically implanted in the apices of both horns, 34 percent of the zygotes migrated to the opposite horn between the 10th to 13th day of gestation.⁷ Intrauterine migration and spacing of embryos in sows is necessary

to fully utilize uterine space and to maintain pregnancy. If only one horn or one-half of each horn is occupied at 12 to 14 days postovulation the sow will return to estrus.^{4,7} At least four live embryos were necessary in sows for pregnancy to be maintained to 40 days.^{4,7} In sheep 7 to 10 percent of zygotes migrated to the contralateral horn when double ovulation occurred on one ovary.³ Embryonic death loss was much greater where both ovine zygotes remained in the same horn after double ovulation from that ovary. This is apparently also true in cows because twin fetuses in one horn are seen in only 10 percent while bicornual twin fetuses are seen in 90 percent of bovine twin pregnancies. The mechanism of the intrauterine migration and spacing of zygotes in multipara is not well understood but probably involves the muscular activity of the uterine wall and the attainment of a certain size of blastodermic vesicle.

Superfecundation is the result of a female ovulating two or more ova during one estrum and copulating with two or more males during that estrum with ova being fertilized by spermatozoa from each male. This condition may be suspected by the breeding history. After parturition it may be obvious because of offspring resembling each sire. Superfecundation is observed more commonly in multipara, especially bitches and queens, because multipara regularly ovulate two or more ova, have long heat periods, and opportunities for services by different males are greater than in unipara. Superfecundation in unipara has occasionally been reported, for example, the birth of twin horse and mule foals and twin calves sired by bulls of different breeds.

Telephony is a superstitious belief prevalent especially among dog breeders that offspring from one sire may derive characteristics from a sire to which the same dam has previously borne offspring. This belief is most commonly recalled when by accident a purebred female is bred by a mongrel and has offspring from this mating. It is then falsely believed that the dam is "tainted" and that even though she may be bred later to a purebred sire the offspring from this purebred mating will have certain mongrel characteristics. There is no basis for this erroneous belief.

Superfetation may occur when a pregnant female, carrying one or more live fetuses comes in estrum, is bred again, and a second conception occurs in a uterus already containing at least one live fetus. This condition is seemingly authentically reported more often in multipara and only rarely in unipara. It appears unlikely that in uniparous animals, even if ovulation occurred, the spermatozoa could pass through a cervix closed by an adhesive cervical seal and through the pregnant uterus to the oviduct. If the ovum was fertilized and reached

the uterus, the endometrial area of both horns would in most instances already be utilized by the first embryo or fetus. If by chance the second zygote should develop in the horn opposite to the one containing the embryo, when the earlier fetus was expelled the later fetus would probably be expelled at the same time. These viscissitudes cause many authors to doubt the occurrence of superfetation in uniparous animals.

Although the literature includes many reports of alleged cases of superfetation, most are unauthentic and lack essential details. Twin foals usually differ in size, one large and one small. The expulsion of unequal sized twins, even though the mare has been bred twice, does not constitute a claim for superfetation. In cases in which one cow in a herd gave birth to twins on pasture with one of the twins being adopted and suckled by a second cow in advanced pregnancy, superfetation is often claimed when this second cow, especially if it had been bred twice at the proper intervals, gives birth later to her own calf. A third condition may possibly occur wherein a cow or mare carrying bicornual twins in separate membranes gives birth to one twin a number of weeks or months before the second.⁸ The first twin is always smaller at birth than the twin born several weeks or more later. Several ewes aborted one of twin fetuses at 105 days of gestation. These ewes then delivered normal lambs at term over a month later.² This phenomena, although rare, has been reported in cows, sows, ewes and women as **double parturition**. It seems a more logical explanation for the birth of young at different periods following conception than does superfetation.¹²

In multiparous animals with a poorly defined cervix and cervical seal, superfetation is more likely to occur.^{10,11} Two normal feline term fetuses were removed from one uterine horn by cesarean section. A small 5 week-old fetus, 33 mm CR length, was found in the opposite horn of the uterus.⁹ They cited references to indicate that pregnant cats might develop mature follicles and ovulate as late as 6 weeks after conception. All the fetuses of one service could develop in one horn and then subsequently an estrum occur with ova fertilized from the second service developing in the opposite horn. Parturitions could occur at different times from each horn. This is unlikely as in double parturition in swine, fetuses are expelled from both horns at each farrowing period.¹⁴ This possibility might occur in cows with a true uterus didelphys or double uterus with a separate cervix for each horn. In the apparently authentic bovine case reported to the author, a double uterus was not present.⁴

Although superfetation may occur very uncommonly in multipara and rarely in unipara, it would appear highly improbable in most reported instances. Many reports on

superfetation are obviously incorrectly diagnosed without proper information and sufficient detail on which to base a claim. A few rare reports, however, appear sufficiently authentic to make one unwilling to state positively that superfetation does not occur in domestic animals, especially sows and cows.

Pseudopregnancy in the bitch and queen—False pregnancy or pseudocyesis is common in the bitch because the metestrus, luteal, or postestrus phase of the cycle is about 8 to 9 weeks long, or approximately the same duration as pregnancy.² During this metestrus period in the bitch the endometrium resembles that in pregnant bitches. The corpora lutea are large and active during postestrus but gradually reduce in size and become inactive at 8 to 9 weeks after estrum or sterile coitus. At this time many bitches exhibit mammary development and may lactate if nursed. The mammary development is not as great as in pregnant females. Toward the end of pseudopregnancy, false pregnancy or pseudocyesis certain bitches, especially the smaller breeds, may be nervous, aggressive, excitable, restless or withdrawn and may even exhibit "phantom whelping" by preparing a "nest" and mothering and protecting some inanimate object. Often bitches in pseudopregnancy will put on weight and their abdomen will increase in size. Most bitches do not exhibit these signs. If the symptoms at the termination of this period are objectionable to the owner, small doses of estrogen or testosterone may possibly aid in hastening the return to normalcy. The use of tranquilizers in the affected bitch may reduce the objectional behavior patterns during this transient period. In most affected bitches these symptoms tend to recur following each estrum so ovariectomy may be considered unless the bitch is to be bred. In the queen pseudopregnancy or metestrus lasts about 30 to 40 days but without noticeable signs.

Miscellaneous Fetal Patterns and Lactation

Although the rate of growth and body characteristics of the fetuses of domestic animals have been described in this and preceding chapters, other fetal developmental patterns and activity occur that should be noted.^{16b} Since the weight of male bovine fetuses and the uterus were heavier, and cotyledon, placenta and fetal fluid weights were not influenced by the sex of the fetus, it was concluded the uterus increases in size to accommodate the size of the fetus and that the size of the uterus has no influence on fetal size.²²

Blood flow to the bovine uterus, as measured in the uterine artery to the gravid horn, increases from 120 ml/

min. at 40 days, to 205 ml/min. at 90 days, to 1960 ml/min. at 145 days, to 3200 ml/min. at 188 days, to 3900 ml/min. at 215 days of gestation. Utero-ovarian vein blood flow in ewes at 120 days of gestation was about 1350 ml/min. with twin pregnancy and about 1750 ml/min. with triplet pregnancy. Thus in both of these studies uterine blood flow and nutrient uptake were closely related to the amount of uterine, placental and fetal tissue.^{3,11}

Fetal movements or kinesis occurs throughout the greater part of pregnancy and has been studied by ultrasonography. Simple movements were detected from 90 days of gestation in the equine fetus and averaged 9 movements per 10 minutes. Later in gestation movements became more complex and lasted longer, especially during the prepartum period. This activity is necessary for the normal development of muscles and joints and to assume the correct posture for birth.¹⁵ Ovine fetuses of 109 to 143 days of age swallowed 100 to 500 ml. of amniotic fluid daily during two to seven random episodes. Since from about 115 days the ovine fetus produces thick mucoid oral and tracheal secretions and its mouth and pharynx are always filled, the factors initiating these swallowing movements is not known.²

In the bovine fetus, as other species, lymphocytes develop first in the thymus by 50 days then by 175 days in all the peripheral sites. Associated with this lymphoid development was the ability to mount an antibody or immune response or become immunologically competent depending upon the nature of the antigen. This varied from 100 to 250 days of gestation with many bovine bacteria and viruses.^{16b,25}

Although the mammary gland is a highly modified and specialized sebaceous cutaneous gland, it is normally considered to be an accessory gland of the reproductive system because of its intimate association with reproductive functions and hormones. In domestic animals the mammary secretion provides early passive immunity to the newborn as well as supplying its nutritive needs. In the cow most of the immune globulins transferred from the blood to the udder secretion or colostrum takes place a short time before, during and after parturition whether the cow has been premilked or not. If the cow or mare has been premilked or the colostrum has leaked from the udder the level of globulins present per unit of lacteal secretion is reduced.^{20,24} In the mare, cow, ewe, and doe, the mammary gland is located in the inguinal region. In the mare, ewe, and doe the gland is divided into two halves with a single lactiferous sinus in each half opening into the two teats. In the cow the udder is divided into four quarters, each with its own lactiferous sinus and teat. Supernumerary teats and glands are common

in the cow. There is no communication between the halves or quarters of the mammary gland. In the sow, bitch, and queen the paired mammary glands are located on the ventral surface of the body in the pectoral, abdominal and inguinal regions. There are from 4 to 9 pairs of glands. The lactiferous ducts or streak canals at the ends of the teats are closed by a sphincter muscle. There is a single streak canal in the teats of cows and ewes but two streak canals in mares and sows. Bitches have 7 to 16 duct openings in the teat. The blood supply of the inguinal mammae is the external pudic arteries, of the pectoral mammae the branches of the internal thoracic arteries, and of the abdominal mammae from both sources. In the cow the main veins of the udder are the external pudic and the subcutaneous abdominal or "milk" vein. The latter empties into the internal thoracic veins. A well-developed lymphatic system is also present in mammary tissue.²⁸ The nerve supply to the mammary gland is the inguinal nerve from the ventral branches of the second through fourth lumbar nerves. The mammary branch of the internal pudendal nerve supplies the caudal part of the bovine udder. The motor nerve supply to the udder is entirely autonomic or sympathetic; the cell bodies of these nerves are located in the lateral horns of the spinal cord. Superficial innervation and blood supply of the skin of the udder comes from the subcutaneous vessels and nerves in the skin regions surrounding the udder.

Relatively little mammary development occurs before puberty. In the newborn, slight mammary and teat development is noted along with a slight amount of serous secretion. This is probably due to the placental transmission of some of the circulating maternal steroidal hormones. In rare cases this may be marked in dairy calves. There have been a few instances of dairy heifers 5 to 12 months of age or older that developed marked mammary development with milk secretion. The cause is usually not known. Granulosa cell tumors of the ovary or the consumption of estrogenic mycotoxins may rarely be the cause. Suckling by other heifers causes udder growth and an increase in the amount of milk secretion. After isolation, the mammary development of the heifer will recede spontaneously within four to six weeks. With the onset of estrual periods after puberty there is a slight mammary development. In animals exhibiting pseudo-pregnancy such as the bitch, mammary development may be quite marked and be nearly equal to the development in the pregnant bitch, and milk secretion will occur.

During the first half of gestation in the cow cellular proliferation of the mammary ducts and alveoli occurs under the influence of the steroid hormones, progesterone and estrogen, from the ovaries and the placenta. By the fifth month growth of the secretory tissue is nearly

complete. During the latter half of gestation cellular hypertrophy and limited secretion is noted. Abortion after the middle of gestation followed by regular milking of a cow or heifer results in lactation. The nearer to the calving date the abortion occurs the greater the production of milk. The failure of animals to reach high levels of production after an abortion is due to insufficient hormonal stimulation for milk secretion rather than to incomplete development of the mammary gland.²³ In the normal high-producing heifer or young cow excessive edema or engorgement of the mammary gland and the adjacent skin and tissues dorsal to the udder and forward on the abdominal floor to the xiphoid region may occur. This is apparently a circulatory phenomena caused by a greater blood supply to the gland than the venous system can accommodate. Excessive edema of the abdominal floor is sometimes confused with rupture of the prepubic tendon, umbilical hernia, a hematoma, or an abscess. Occasionally the greatly enlarged and edematous mammary gland may cause pain and discomfort, necrosis of the skin, failure to let down milk and stretching or even rupture of its supporting ligaments. Massage, the use of mild counterirritants, premilking, udder supports, cold and hot applications, and controlled exercise may be used to prevent or treat excessive udder edema. (See Figure 58.)

In recent years the oral or intramuscular administration of diuretics, specifically the carbonic anhydrase inhibitors with or without corticosteroids, for udder edema after parturition has been particularly helpful especially in young cows with a physiologic edema. These treatments are usually given for one to 3 days.²¹ Large doses or prolonged intake of lower doses of the glucocorticoids late in gestation may cause premature parturition often associated with retention of the placenta in cattle. The level of grain feeding, before parturition, whether high or low, had no influence on the degree of udder edema that developed.^{17,26} However, high prepartum grain feeding increased slightly the udder edema in heifers but not in cows.⁸

Mammary growth and lactation is mainly under the control of hormones.^{4,9} Nerves in the teats and skin of the udder may play an indirect part in milk secretion by stimulating the pituitary gland to release prolactin and possibly other hormones necessary to initiate and maintain lactation and oxytocin necessary for milk-ejection or "let-down." This latter term by signifying the ability of the animal to control her milk flow at will is incorrect.^{13,14} Vasomotor nerves probably play an indirect role in milk secretion by regulating the blood supply to the gland. Inguinal nerves have been cut without producing any change in milk production. Estrogens and proges-



Figure 58. Udder and subcutaneous edema in a parturient heifer. (Courtesy D. Morrow.)

terone produced in the ovaries and in the placenta work together in animals to cause mammary development. The estrogen causes the initial budding and the growth of the duct system. Progesterone causes further duct growth and alveolar development. In certain species, such as does, estrogen alone induces complete udder growth and lactation but some of the female's other endocrine secretions probably play a role.

The onset of lactation at the time parturition coincides with the drop in progesterone and estrogen levels in the blood that have provided for mammary growth, and with a marked rise in the levels of prolactin or lactogenic and growth hormone from the pituitary gland necessary for the initiation of milk secretion and maintenance of lactation. High prolactin levels are favored by the mammary stimulation of suckling and removal of colostrum and milk from the alveoli of the mammary gland except in sheep and goats.⁷ Prolactin secretion is usually initiated toward the end of gestation and rises rapidly just before and after parturition. Growth or somatotrophic hormone is also very important in the initiation and stimulation of lactation in cows. Oxytocin released by suckling might be closely associated with or cause the release of prolactin and growth hormone, STH, from the anterior pituitary gland. In most domestic animals suckling of young prevents or delays the onset of postpartum estrus compared to females whose young were weaned soon after parturition. This is especially noted in beef cows that suckle their young, especially twins, compared to dairy cows who don't. This delayed onset of postpartum estrus in suckled females is not due to lactation per se but is possibly due to the stimulus of repeated daily suckling that causes a reflex secretion of cortisol and prolactin that exert an antigonadal action by

suppression of the gonadotropic hormone, LH. Further study is necessary to elucidate the exact effects of frequent periods of suckling on the endocrine and reproductive systems.^{4,7,7b,17b} Low levels of administered estrogens aid in the release of prolactin and stimulate milk production.³¹ This may account for the drop in milk production in high-producing cows following treatment for cystic ovaries.

Normal lactation requires mammary development during pregnancy by hormonal stimuli. These stimuli comprise a complex of mammogenic hormones including progesterone, estrogen, relaxin, growth hormone, prolactin, corticosteroids and placental lactogens.^{7,9} Placental lactogens have potencies similar to prolactin and growth hormone and were found in bovine, caprine and ovine plasma. In the former, levels were low until 160 days of gestation and then increased to 200 days and plateaued until parturition. In the doe evidence was presented to indicate that does carrying twins or triplets had a higher milk yield due to the increased production of placental lactogen than occurred in single births.^{8b} The actual initiation of lactation requires low progesterone and estrogen levels and a high prolactin level such as occurs immediately postpartum. Maintenance of a high level of milk production requires oxytocin, prolactin, growth (STH) hormone, adrenal corticoids and parathyroid hormones.^{20b}

An enormous amount of work is performed by the lactating udder in the high-producing cow, 450 volumes of blood are required to produce one volume of milk. Dairy cows require an optimal length of 40 or more days dry period. Dry periods shorter than 40 days in length resulted in over a 1000 lbs less milk the following lactation.^{4b}

Thyroid stimulating hormone, TSH, has a galactopoietic effect. Thyroxine or other similar substances such as iodinated casein (**Protamone**) also have a galactopoietic effect on lactation. The daily feeding of iodinated casein or thyroprotein with a 3 percent throxine potency at a level of about 1 gram per 100 lbs. of body weight to lactating cows has caused increases in milk production and butter fat of 5 to 25 percent depending upon the cow's genetic constitution and the level of feed intake.¹⁶ Increased intake of T.D.N. or energy is essential in most treated cows. Since not all cows respond equally, individual supervision of cows is necessary. Milk records of cows on thyroprotein are not officially recognized by the Dairy Herd Improvement Assoc. If thyroprotein is removed suddenly from the ration a marked drop in milk flow usually occurs. Although a few well managed dairy herds have had good results by the properly supervised use of this product, many herds have experienced poor

results. In properly-conducted experimental long-term trials the use of thyroprotein has not appeared promising. Some dairymen are using this product selectively to boost production in cows the latter half of lactation when the cow's production declines below 40 pounds per day to prevent a prolonged dry period.

The artificial or hormonal induction of lactation in cattle and to a lesser degree in ewes, does, and laboratory animals has been the subject of much experimental work over the past 30 years.^{9,15b,17c,20b} Nulliparous cattle have given a much more uniform and satisfactory response than have sterile pluriparous cattle. The general technique consists of administering by injection or implants estrogen, estrogen and testosterone, or preferably estrogen and progesterone into animals to maintain fairly high daily levels for a period of one to three weeks to promote mammary duct and alveolar growth. After proper mammary growth has been achieved the injections are stopped or the implants are removed and regular frequent milking is started. The quantity of milk secreted is extremely variable between animals and ranged from 250 to 500 ml. daily to amounts normal for cattle after a gestation period. Failure to induce satisfactory lactation appeared to be due to low prolactin production.¹⁸ The response of nulliparous animals is more consistent than multiparous animals but in general this procedure is not satisfactory enough for practical use.

Two complications may be observed in this procedure: The cattle may develop cystic ovaries with symptoms of nymphomania. Fractures of the pelvis and limbs have been reported due to excessive mounting and a marked relaxation of the pelvic ligaments. If cystic ovaries do not occur the ovaries become small and inactive. The suppression of the gonadotropic hormones and ovarian activity is released when the estrogens are withdrawn. If lactating cows are injected with large doses of estrogens lactation promptly declines. If cows are pregnant they often abort due to the long-continued estrogen levels. Fluoroprednisolone acetate (**Predef**) given daily at doses of 10 to 15 mg. for 15 days caused the induction of lactation during gestation in heifers.³⁰

The diverse effect of estrogens on lactation requires further explanation. In therapy for humans, estrogens are widely used in low doses to relieve swollen, engorged breasts or in larger doses to suppress and stop lactation. This effect is evident when estrogen is used toward the end of pseudopregnancy in bitches with mammary enlargement. Most veterinarians are fearful of causing a decline in milk production with estrogen therapy to reduce milk flow and relieve udder congestion in domestic animals after parturition. Almost all such cases generally respond to less heroic therapy. In the preceding para-

graph the use of an estrogen was described to promote mammary growth and lactation. In the nonlactating cow estrogen at low, prolonged levels promotes mammary growth and development. While this is occurring, secretion is slight. The high blood levels of estrogen must drop so that the full secretion of milk may begin, since maximal growth and secretion cannot occur simultaneously. Prolonged high estrogen levels may suppress or hold in check the pituitary secretion of prolactin and growth or somatotrophic hormone or more likely effect the mammary tissue so it can't respond to the stimulus of the anterior pituitary hormones necessary for lactation. When this estrogenic check is removed the pituitary hormones are released and lactation results. At the time of estrum a slight drop in milk production often results due to the increased restlessness and nervousness of the cow at this period as well as to the decreased feed intake and the increased estrogen production from the follicle. In most pregnant dairy cows the gradual increase in estrogens produced by the placenta from the fifth month to term together with the increased nutritive needs of the fetus, tend to result in a regular decline in milk production. Sterile high-producing cows may lactate at a high level for two or more years. There is no evidence or proof that ovariectomy of lactating cows has any influence on prolonging lactation or increasing production.² Some cows and mares may be difficult to "dry off" because of the high production of milk 10 or 12 months and 5 or 6 months, respectively, after parturition. Marked temporary reductions in nutritive intake and water together with gradually prolonged periods between milkings will involute the mammary glands of domestic animals.

The ejection or "let-down" of milk which is closely associated with the reproductive organs and their hormones, is caused by stimuli, such as suckling, milking or massage of the udder and teats and conditioned stimuli developed by routine premilking barn procedures that effect a release of oxytocin and vasopressin from the posterior pituitary gland by means of neural stimuli acting on the hypothalamus. These hormones are carried to the udder by the blood stream and cause contraction of the myoepithelial cells around the alveoli and ducts. Vasopressin exhibits about 20 percent of the milk-ejection activity of oxytocin.^{13,14} This results in an increase in intracistern pressures from 15 to 20 mm. up to 30 to 45 mm. of mercury with distention of the teat and gland cisterns with milk.⁴ Oxytocin was released transiently and at low levels, about one-twentieth to one-tenth of a unit, to cause milk let-down in a cow within about 40 to 50 seconds. The elevated intramammary pressure was maintained for about one hour unless the cow was milked.

The half-life of oxytocin in animals is quite short, only one to two minutes. The posterior pituitary glands of does and cows contain about 10 to 15 and 30 to 50 units of oxytocin, respectively.¹⁹ The effectiveness of the expulsion reflex is transitory and prompt removal of the milk is desirable for effective proper milking. This neurohormonal reflex mechanism is suppressed by excitement, noise and fright which cause the secretion of adrenalin or epinephrine. This failure of milk let-down was probably due to a central block of the release of oxytocin from the hypothalamus and pituitary gland rather than to an inhibitory effect exerted by adrenal stimulation.⁶ Adrenalin caused vasoconstriction and reduced the blood supply and the amount of oxytocin to the myoepithelial cells in the udder.² The release of oxytocin does not occur at milking time in goats and is not essential for the complete milking of the goat udder.^{13,14} The understanding of this mechanism is helpful in cows in developing a proper, relaxed, quiet, regular procedure of milking that results in good milk ejection and rapid and prompt evacuation of the mammary gland. Prolonged milking caused by improper milking procedures results in loss of time, loss of milk, greater rate of involution of the mammary gland, and decline of milk production, besides favoring mastitis in chronically-infected glands. In certain heifers with greatly engorged and painful udders after calving, ejection does not occur, due to the pain and irritation of the swollen edematous udder. These cases benefit greatly from the intravenous or intramuscular injection of 5 to 15 units of pituitrin or oxytocin, and the prompt removal of the milk as the injected hormone rapidly induces milk let-down. These recommended low doses of oxytocin are in reality massive when compared to the physiologic amounts released by posterior pituitary gland. In cows given an intravenous dose, this let-down occurs within one to two minutes; in intramuscular doses it occurs within four to six minutes. The ejection of milk can frequently be stimulated by massage of the uterus, vagina or intrapelvic structures per rectum. It may be noted at the time of removal of a retained placenta, or in performing an infertility or pregnancy examination. It is also observed on vaginal or vulvar examination in cows and mares. Mares may exhibit milk ejection and leaking of milk just prior to, during or after coitus with a stallion.

Milk is produced by a true secretory process. The initial portion of bovine milk at a milking has a low fat content of about one percent while the "strippings" have a ten percent fat content. Most of the milk given at a single milking is present in the udder at the time of milking. In high-producing cows this causes a stretching of the udder tissues, and an intramammary pressure devel-

Table 8. Composition of Milk in Percent in the Domestic Animals*^{1b, 10, 28}

	Water	Fat	Protein	Lactose	Ash
Cow	86.2	4.4	3.8	4.9	.7
Ewe	82.9	6.2	5.4	4.3	.9
Goat	87.1	4.1	3.7	4.2	.8
Sow	83.0	7.0	6.0	4.0	.9
Cat	82.0	5.0	7.0	5.0	.6
Dog	79.0	8.5	7.5	3.7	1.2
Horse	89.0	1.6	2.7	6.1	.5
Man	87.4	3.8	1.6	7.0	.2

ops which suppresses further secretion. Thus in high-producing cows more frequent milking yields greater amounts of milk per day. Cessation of milk secretion or "drying off" is accomplished by allowing the intramammary pressure of milk to increase and remain high for four to five days. A six to eight week dry period between lactation periods is essential in cows for maximum milk yield. In most cows a shorter dry period is accompanied by a 20 to 30 percent decline in milk production the following lactation period.^{25, 29}

The average composition of milk in domestic animals is given in Table 8.

The amount of milk produced by domestic and wild animals varies greatly between species, breeds, individual animals, the level of energy intake, the quality and amount of protein and the amount of minerals, salt and water intake.^{1b} Environmental, management and disease factors play an important role in determining the amounts of milk produced. In general, cows produce 25 to over 100 pounds daily, mares 20 to 50 pounds, goats 3 to 15 pounds, ewes 2 to 10 pounds and sows 5 to 20 pounds daily.

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Sex Parity and the Bacterial Flora of the Pregnant Uterus

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Chapter V

DISEASES AND ACCIDENTS OF THE GESTATION PERIOD

Abortion

Abortion is defined as the expulsion of a dead conceptus or a living one incapable of independent life at any period of gestation. Pregnancy wastage or losses occurring during the period of the early embryonic period, or even during the late embryonic or early fetal period are usually unobserved and unrecognized and economically are not as serious as abortions late in gestation. These early large losses are usually considered to be infertility since conception appears to have failed to occur. These losses will be discussed under infertility in subsequent chapters. Preterm births of immature viable fetuses are called **premature births**. With proper care and nursing, some immature newborn can be raised. By common usage dead fetuses expelled at term are called **stillbirths** (See Chart I). The phrase "born dead" is improper.

Economically and emotionally mid term or late abortions are of great concern to the owner whether the animal is on a commercial or hobby farm because the fetus(es) are lost, the unproductive female must be maintained for a long period or sold at a loss, a prolonged period of uterine disease and infertility or sterility may follow, and if the cause of the abortion is infectious, the disease threatens the rest of the herd.

The many agents causing abortion may be categorized into groups that include: physical causes (hyperthermia, trauma, hypoxia); genetic causes; environmental causes (nutritional deficiencies, toxic plants, agents, chemicals or drugs); hormonal causes (excess estrogens, prostaglandins and cortisol, and progesterone deficiency); and infectious causes (viral, bacterial, fungal, protozoal, and others). Prior descriptions of teratogenic agents producing disease of the embryo or fetus of the domestic species of animals should be noted (See Chapter III). The ingestion or exposure to large amounts of these agents often caused the death of the embryo or fetus and abortion. Lethal or semilethal defects were often observed at birth or in the postnatal period whether due to these toxic agents, nutritional or genetic causes. (See Chart I and teratogenic anomalies and infertility.) These multiplicity

of agents may act singly or in various combinations to result in abortion.

Death of the conceptus usually results in abortion. But in the embryonic or early fetal period maceration and resorption may also occur (See Figures 59 & 60). During the early fetal or second trimester of gestation fetal death may be followed by mummification in all domestic animals, especially the multipara. Maceration of a dead or mummified fetus may rarely occur during the first or second trimester with an accompanying pyometra. Fetal emphysema may occur during an abortion in the late second or third trimester, or dystocia in premature or term birth.

In most abortions during the second and third trimester the fetus is autolyzed because fetal death usually occurs 2 to 5 days before expulsion. This postmortem fetal decomposition is characterized by grey or cloudy corneas observed about 12 hours after death. At 24 hours the kidneys become soft and pulpy and the abomasal contents are cloudy, mucoid and often flocculent. At 36 to 96 hours after fetal death the subcutis is gelatinous and reddish or blood-tinged, the liver is soft and friable and the abomasal contents are reddish.⁸ Diseases of the fetus and placenta do not always result in fetal death. Neonates may be born prematurely or at term and be weak and diseased and die shortly after birth or survive.

Further studies are needed to explain the various mechanisms of bovine abortion or fetal mummification after fetal death. Prostaglandin blood levels increase 5 to 10 fold in cows just before abortions, accompanied by a sudden decline in blood levels of progesterone probably due to the involution of the corpus luteum,^{2a,2b} similar to that occurring just before a normal parturition. Further studies on uterine contraction and cervical dilation and blood levels of estrogen and cortisol are indicated.

It is apparent that many of the causes of abortion in domestic animals are not yet known and the pathogenesis of many known causes is not understood even though in the past 20 years many studies have discovered new causes of abortion and new knowledge concerning the known causes. During this period much research on the

viral causes of fetal disease has occurred. The affinity of rapidly growing fetal and placental tissues for viral multiplication is evident. The cellular and humoral aspects of the immune response develop sequentially in the fetus. Infection prior to immune competence may result in abortion, fetal malformation, and occasionally viral persistence and immune tolerance. Immune responses, if they occur, cause an elevation of immunoglobulin and antibody in the fetus. The latter may be of diagnostic value.^{23b}

Even with these many studies, the actual incidence of abortion in the various domestic animal species is not known. Nor has the relative importance or incidence of the various etiologic agents of abortion in each species been established. Even when a freshly aborted fetus and placenta and maternal blood sample are promptly and properly collected, stored, refrigerated or frozen and delivered with a complete and carefully documented history and clinical report to a highly competent diagnostic laboratory with trained microbiologists, pathologists, toxicologists, immunologists and electron microscopists less than 50 percent confirmed diagnoses are made. One important reason for the difficulty in making a laboratory diagnosis of abortion is the autolysis that occurs in most aborted fetuses prior to expulsion.

A variety or battery of diagnostic serologic tests have been developed to screen or test blood samples from the dam and fetuses after expulsion for bacterial and viral diseases associated with abortion. It may be desirable in some instances to take a second blood sample from the dam two to three weeks later to see if a rise in titer occurs, that might explain a recent bacterial or viral infection. However, testing of paired serum samples seldom provided helpful or valid results.⁶ Furthermore up to three or more positive serological tests for different viral antibodies were noted in the plasma or fetal fluids of most aborted fetuses. Undoubtedly the dams' plasma would reveal similar antibodies.^{9,10,21a,b,22} A positive serologic test of the aborted fetus or dam for antibodies against an abortifacient, infectious agent does not indicate when the infection occurred or if that agent was responsible for that abortion. In fact in IBR abortion late in gestation the fetus usually dies rapidly before antibodies can be produced.^{16a,b} Also nearly all bovine infectious organisms can infect the fetus *in utero* causing the production of antibodies whether or not abortion occurs.

Thus viral, bacterial or other serological determinations have serious diagnostic limitations and require interpretation with history, clinical signs, necropsy and isolation of infectious agents. A serological diagnosis is a retrospective aid and seldom provides answers of immediate use in outbreaks. Antibodies may result from

prior infection, vaccination, colostral antibodies, or cross-immunity reactions. The presence of antibodies in the serum of aborted fetuses indicates prenatal infection but does not indicate that infectious agent produced the abortion. Conversely failure to detect antibodies in a fetus does not eliminate that agent as a cause for the abortion.^{15b}

Bacterial, viral, fungal and protozoal cultures of the organs of the aborted fetuses, the placenta, the amniotic fluid, the uterus and the dam's vagina and urine may be taken. Gross and microscopic examinations of fetal and placental tissues that are not autolyzed can be made for bacteria, viruses or fungi and pathological lesions including intranuclear inclusion bodies. Specific fluorescent antibody tests are also helpful in diagnosing certain viral and bacterial diseases in partially autolyzed tissues of the fetus or placenta.¹⁷ A careful histopathological examination of fetal organs and tissues and the placenta, if autolysis is not advanced, is one of the most useful and informative procedures in diagnosing the cause of abortion. Abortion is primarily a disease of the fetus not the dam, and the placenta as an organ of the fetus should also be carefully examined.^{16a} A complete reproductive and health history of the affected animals and the herd is necessary and helpful in making a diagnosis. This should include records of the type, brand and date of vaccinations of the dam and any medications given the dam. A history of the ration, grain, forage and minerals fed the cows and herd including any possible access to drugs, poisonous plants and toxic chemicals. Certain endocrinological and toxicological tests may be indicated. Infections may not be the cause of the largest group of abortions but it is most frequently diagnosed.

Such careful competent tests of each aborted conceptus submitted costs about \$150 per specimen. With only a 25 to 50 percent rate of probable diagnoses, the total cost for each positive diagnosis would be \$300 to \$600. When one considers that a careful interpretation of tests is necessary to be certain a positive serological result actually was related to the abortion and a positive culture does not necessarily mean the recovered agent caused the abortion, the justification of such costly testing might certainly be questioned for many cases of abortion.¹⁶ This underlines the great need for adequate research to accompany diagnostic efforts in this important area.

Sporadic causes of abortion are more difficult to diagnose than epizootic abortions since present knowledge and laboratory procedures are of little assistance in diagnosing non-infectious abortions due to toxins, genetic defects, nutritional deficiencies and hormonal deficiencies or excesses.^{17,18} If an epidemic of abortions is occurring in a herd, the cause is more readily diagnosed. It is common practice to accept an incidence of 3 to 4 percent of

abortion in a herd. Therefore, if several abortions have occurred before a diagnosis is attempted, the disease, if epizootic, may have spread through the herd unless diagnosed promptly with the first abortion.

The incidence of pregnancy wastage or losses, based on limited data is in the range of 30 to 40 percent in cattle, with a 7 to 12 percent of incidence of abortion in cattle after they were diagnosed pregnant by rectal examination at 30 to 50 days.^{5,21,22}

Although direct trauma per rectum to the embryo or young fetus and manual removal of the bovine corpus luteum may cause its death and resorption or abortion, external trauma to either man or animal seldom results in abortion.¹⁴ It is a common misconception by laymen that external injuries or trauma can readily cause abortion in animals.

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Abortion in Animals

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Abortion in Cattle

Because of the multiplicity of agents causing abortion in cattle, an incidence of 2 to 5 percent sporadic abortions in a herd are common and expected in an area free, or with a very low incidence, of bovine brucellosis. When the incidence exceeds 5 percent most owners become se-



incidence of abortions, stillbirths and postnatal deaths were 2.1, 5.9 and 3.2 percent, respectively. Lesions related to anoxia were found in 73 percent of all stillborn fetuses. Stillbirths were higher in primipara than multipara, 9.3 vs 3.7 percent, and in unattended births than in those that were monitored, 9.4 vs 2.7 percent, respectively.^{11b}

Brucellosis (Contagious or Infectious Abortion, Bang's Disease) is caused by a small gram-negative coccobacillus, **Brucella abortus**, that grows intracellularly. It

Table 9. Summary List of Causes of Abortion in Cattle

Infectious Causes

Bacterial—Brucellosis (**Br. abortus**), Leptospirosis (**L. pomona**, **L. hardjo** and others), Listriosis (**L. monocytogenes**), Salmonellosis (**S. typhimurium**, **dublin** and others), Campylobacteriosis (**C. fetus venerealis**), Tuberculosis (*Mycobacterium bovis*) miscellaneous bacteria, and other organisms, streptococci, diplococci, staphylococci, *E. coli*, *C. pyogenes*, *Erysipelothrix rhusiopathiae*, *C. fetus intestinalis*, *Alcaligenes fecalis*, *Pseudomonas aeruginosa*, *Mycobacterium avium*, *Pasteurella multocida*, *Nocardia asteroides*, *Mycoplasma bovis* and *agalactiae* var *bovis*, *B. cereus*, *Hemophilus somnus*, *Yersinia pseudotuberculosis*, *Serratia marcescens*, *Spherophorus necrophorus*, *Rickettsia* (*Ehrlichia phagocytophilia* Tick-borne fever), *Coxiella burnetii* and *Chlamydia* spp.

Viral—Infectious Bovine Rhinotracheitis (IBR-IPV), Bovine Virus Diarrhea—Mucosal Disease (BVD-MD), Miscellaneous viruses—Myxovirus parainfluenza 3, bovine enteroviruses, bovine parvovirus, Bluetongue virus (BT), and Pseudorabies, Malignant Catarrhal Fever, Akabane, Foot and Mouth Disease, Rinderpest, Rift Valley Fever and Bovine Infectious Petechial Fever Viruses.

Mycotic or Fungal—Aspergillosis (*Aspergillus* spp.), *Mucorales* spp., *Allescheria boydii*, *Torulopsis glabrata*, *Mortierella wolfii*, *Absidia ramosa*, *Cephalosporium*, and the yeast *Candida tropicalis*.

Parasitic protozoal—Trichomoniasis (*T. fetus*), anaplasmosis (*anaplasma marginale*), Toxoplasmosis (*T. gondii*), Besnoitiosis (*B. besnoiti*) and Babesiasis.

Noninfectious Causes

Chemical, drug and poisonous plants—nitrates, chlorinated naphthalenes, arsenic, locoweed (*Astragalus* and *Oxytropis*), perennial broom weed, pine needles, sweet clover hay, mycotoxicosis, polybrominated biphenyls (PBBs).

Hormonal—estrogens, glucocorticoids, prostaglandins, progesterone deficiency.

Nutritional—starvation and multiple deficiencies including vitamin A, iodine and selenium deficiencies.

Physical—infusion or insemination of the pregnant uterus, rupture of the amniotic vesicle, crushing embryo or fetus, decapitating fetus, removal of corpus luteum, torsion of uterus or umbilical cord, stress due to work or fatigue, disease, transport or major surgery.

Genetic or Congenital—defects of embryo or fetus, chromosomal or genetic abnormalities.

Miscellaneous—twinning, allergies, tumors, adhesions of uterus, endometrial deficiencies.

was first described in Denmark by Bang in 1897. It is the most important worldwide cause of abortion in cattle except in countries such as the U.S. where the widespread use of strain 19 vaccination has been incorporated into a control program to greatly reduce the incidence of the disease. Brucellosis has been well-described.^{4,11,15}

Br. abortus causes abortion in cattle during the last trimester of pregnancy and a subsequent period of infertility is usually experienced. The disease is also important because **Br. abortus** causes undulant fever or brucellosis in man from drinking raw or improperly pasteurized infective milk or more commonly from exposure to infective discharges or tissues. Farmers, packing house workers and veterinarians are high risk groups. The medical procedures to follow after the accidental injection of **Br. abortus** strain 19 into humans have been reported.¹⁸

Br. abortus is mainly infective for cattle but occasionally other species of animals such as sheep, swine, dogs, donkeys, horses and humans may become infected and abort.^{11,20} In horses **Br. abortus** and *Actinomyces bovis* are commonly present in poll evil and fistulous withers. A high incidence of brucellosis has been reported in herds of bison and elk but the incidence in white-tailed deer and other wild ruminants is low. **Br.**

abortus has been reported in many free-living or wild animals.^{11,20}

The organism is rapidly destroyed by disinfectants, sunlight, drying, putrefaction, and pasteurization but may survive for several months in a moist, cold environment. The **Br. abortus** organism is found in the chorion of the placenta where it produces severe pathologic changes including necrosis and edema and causes severe pneumonic lesions in the fetal lungs. It is often recovered from the stomach contents of the fetus. It also is found as a persistent infection in the udder and the supramammary lymph nodes of adult cows and in the testes, epididymides, vasa deferentia and the vesicular glands of bulls. After abortion the organism does not persist in the uterus and disappears in about 4 weeks as apparently it grows well only in the fetal placenta.¹⁶ The sugar alcohol, erythritol, present in the placenta and male genital tract is a strong growth stimulant of **Br. abortus** accounting for its localization in these tissues.¹¹ Persistently infected udders, which are common in infected cows, appear clinically normal. Occasionally *Brucella* organisms persist in joints or bursae. Infections and blood titers in calves or immature cattle seldom persist as they do in sexually mature cattle. However it has recently been demonstrated that 2 to 3 percent of calves born to in-

infected dams can persistently harbor infection acquired *in utero* or from ingesting infective milk. These calves may be serologically negative until their first pregnancy when they may abort or calve and develop a blood titer and be a source of the spread of *Brucella* organisms to other cattle.⁴⁰

Infection is usually introduced into susceptible herds by the purchase of an infected cow. The incubation period, whether from the time of exposure until a positive serologic reaction occurs or until abortion or parturition when organisms are discharged, varies widely depending upon the age of the animal, the stage of gestation, the exposure dose, the vaccinal status and other factors.^{33b} With massive exposure, positive serologic reactions usually occur in 21 to 42 days. With other degrees of exposure, abortion or parturition with an infected conceptus, may have an incubation period of 53 to 251 days.³⁷ Further evidence of the unreliability of serologic tests as an indication of *Brucella* infection was the report that 13.3 percent of cows aborting culture-positive fetuses were serologically negative at the time of abortion.³² Thus, the variable incubation period and difficulties of diagnosing infection until after probable transmission to susceptible herdmates create serious technical problems in the understanding of the epidemiology and the development of control measures for brucellosis.²⁶

Infection with *Br. abortus* occurs most frequently by the ingestion of genital discharges of aborting cattle that contaminate the feed and water. Transmission may also occur through the mucous membranes of the eye and by intrauterine artificial insemination of infective semen. One infected bull whose semen was used for artificial insemination infected 71 percent of the cows and brucellosis appeared in 41 previously brucella-free herds.³ There is little evidence to show that brucellosis is spread from an infected bull to susceptible cattle by natural service.¹⁷ Calves nursing infected cows may spread the disease by fecal contamination of food ingested by susceptible animals. Occasionally *Br. abortus* may be spread by discharges from fistulous lesions of horses or possibly by quarter to quarter spread of organisms as occurs in mastitis.^{11,15} Once infection occurs in sexually mature cattle about 85 percent remain infected for their lifetime.

Abortions due to *Br. abortus* usually occur from the 6th through 9th month of gestation and premonitory signs of udder enlargement and vulvar edema often are present. The incidence of abortion will vary from 5 to 90 percent in a herd depending upon the number of susceptible pregnant cattle, the rate of transmission, the virulence of the organism and other factors.

The fetal membranes are edematous, hemorrhagic, leathery and necrotic and often there is a brownish-yel-

low pasty exudate in the uterochorionic space. Retained placenta and metritis with a subsequent period of genital discharge and infertility are common sequelae. After one abortion most cows have normal pregnancies but a few cows may abort two or three times. Infected fetuses may be born alive but many are weak and premature and die within a few hours. The dead fetus may exhibit some autolytic changes of edema and hemorrhages of the tissues and body cavities and the hair and skin may be stained with meconium. The most outstanding fetal lesion is bronchopneumonia. If a severe fetal pneumonia is present brucellosis should be suspected.¹⁹

A diagnosis of brucellosis requires laboratory tests that include:

(1) Isolation of the organism from the fetal lungs, stomach or placenta. In adult cattle organisms may be recovered from the milk or semen, or from lymph nodes after slaughter. Fluorescent-antibody staining is of diagnostic value for examining contaminated fetal or placental tissues or discharges from the uterus.¹¹

(2) A number of serologic tests have been developed to detect agglutinating antibodies in the blood of cattle. These tests have recently been reviewed^{33a} and include:

- (a) The tube agglutination test.
- (b) The rapid plate agglutination test.
- (c) The card test, a sensitive screening test that utilizes a low pH stable buffered antigen (in other countries this is called the Rose Bengal test).

These above three tests are considered official tests in the U.S. Other supplemental tests that are useful in distinguishing between naturally-infected cows and cows with vaccination titers include:^{11,30,33}

- (d) The mercaptoethanol (ME) test.
- (e) The rivanol plate agglutination test.
- (f) The complement fixation (CF) test. This test is highly specific for detection of infection.²¹
- (g) Four new tests that have been developed to detect infected cows earlier and are undergoing further evaluation are the ELISA or enzyme-linked immunosorbent assay test, the indirect hemolytic test and the radial immunodiffusion test.^{5,33a} Cell-mediated immune responses to *Br. abortus* and Strain 19 are under study using an *in vitro* lymphocyte stimulation test (LST).^{13,26}

The card test is a sensitive, rapid test for field screening of herds, particularly in range areas. It is superior to the tube test in detecting infected animals.^{26,28} Interpretations of results of official and supplemental tests require proper and knowledgeable evaluations.²⁶ In the official tests noted above a 1:50 reaction in a nonvaccinated cow

is usually considered to be a suspicious reaction and 1:100 a positive reaction. In an officially calf-hood vaccinated cow 1:100 is usually considered to be suspicious and 1:200 is positive. But these standards in an inconstant biological system are not always correct.

Cattle with suspicious reactions to diagnostic tests should be isolated and retested in two to four weeks. There is no practical method at present to distinguish between a serological titer for brucellosis due to vaccination with Strain 19 and infection with a field strain of the organism. The other supplemental specialized serological laboratory tests for brucellosis diagnosis described above are very helpful in problem herds in locating infected cattle that fail to show a reaction to the tube or rapid plate agglutination tests.^{1,28}

Although blood samples in cattle may easily be drawn from the jugular or external abdominal veins, especially in dairy cattle, bleeding from the tail is also simple and rapid and is favored by many in collecting blood samples from beef cattle, bulls and even dairy cattle.⁶ In blood testing cattle one should use proper hygienic precautions so that if anaplasmosis or other disease is present in the herd, the spread of the disease is not favored. The use of market-testing with back tags for identification of beef cattle going to slaughter where blood samples are taken, has proved very valuable in detecting infected beef herds not subject to milk ring test surveillance testing. Cross-reactions in the various diagnostic tests are uncommon. Cross-reactions between brucella, pasteurella and leptospira antibodies were not observed.^{9,29} Serum antibodies provoked by intramammary inoculation of *Yersinia enterocolitica* reacted strongly to the standard test for *Br. abortus*.²²

(3) Agglutination tests on milk include the milk ring test (M.R.T.), or the Brucellosis Ring Test (B.R.T.) for herds and the whey agglutination test for individual cows. In infected cattle in problem dairy herds the efficacy of these tests for the detection of reactor cattle was 92 and 73 percent.²⁸ As a herd screening procedure on bulk milk the M.R.T. is highly successful in indicating dairy herds containing one or more brucella-infected cows. Such detection is followed by blood testing of the individual animals in the herd. The testing of all dairy herds in an area two or more times a year with the M.R.T. has proven highly effective in the diagnosis and elimination of reactor cows.¹¹ After testing over 36,000 cows in 645 dairy herds, periodic blood tests on cattle negative to the milk ring test (M.R.T.) were found to be unnecessary.²⁸ The simple, easily performed ELISA test described above for serum showed promise of being satisfactory for detecting antibodies to *Br. abortus* in milk.¹⁰ This procedure is not applicable to beef herds.

(4) Agglutination tests are highly effective in detecting an increased local antibody level for *Br. abortus* in seminal plasma from bulls³ and in vaginal mucus from cows when an infection is present in the uterus.¹⁴

The herd history is often useful in the diagnosis of the cause for abortion. A differential diagnosis among the causes of abortion may be very difficult and often impossible without good laboratory assistance. The placental lesions in brucellosis, vibriosis and mold or fungal infections in cattle appear clinically similar.

Treatments for brucellosis, including a variety of antiseptics and antibiotics, have been attempted in cattle but with no success because of the intracellular location of the organism. Hygienic measures are essential to a control program within a herd. Infected animals should be sold for slaughter or should be kept carefully isolated at the time of parturition or impending abortion and for a month or more thereafter when the greatest spread of *Brucella* organisms may occur.^{38,39} Aborted fetuses and placentas should be buried or burned and contaminated areas should be disinfected with a 4 percent compound solution of cresol or a similar disinfectant. All cattle coming onto the farm should be tested and isolated for 3 to 4 months and retested before placing with the herd unless they came from a known brucella-free herd. These hygienic procedures are necessary even in vaccinated herds where the field strain of the organism may infect the cow and spread to the udder and lymphoid tissues.

In properly vaccinated cattle, abortions due to brucellosis are uncommon. Vaccination of calves from 2 to 6 or 4 to 8 or 10 months, depending on the various states' regulations based on the incidence of infection, with 2 ml. of freeze-dried, dated, refrigerated, low virulent, reduce-dose Strain 19 *Brucella* vaccine subcutaneously immediately after reconstitution produces a rapid rise in serum antibody titer that recedes in over 90 percent of young prepubertal cattle within 6 to 12 months after vaccination.^{17,26,34} It is imperative that this vaccine be refrigerated and handled properly to assure potency and viability. The immunity in cattle vaccinated with the former larger dose of Strain 19 vaccine at 2 to 6 months of age is equal to that in calves vaccinated at 4 to 10 months of age and lasts in most cattle through their fifth gestation.¹⁷ At the time of vaccination, calves should be carefully restrained and care should be used as Strain 19 can produce brucellosis or undulant fever in man if inoculated subcutaneously or conjunctivally. Vaccination of sexually-mature cattle causes more persistent blood titers and in pregnant cows may rarely cause abortion. In infected herds only 50 percent of calves from infected dams responded to Strain 19 vaccine if vaccinated prior to 95 days of age because of the presence of colostral

antibodies. Calves from infected dams should be vaccinated after 5 months of age.⁷ In a severely infected herd or area, veterinarians may recommend the vaccination of adult cows to prevent severe economic losses by the farmer. This should not be done in an area where eradication or control procedures are being carried out without the approval of state officials. Strain 19 vaccine is the only approved vaccine in the United States. Other vaccines to prevent *Br. abortus* infection such as 45/20 and H38 have been studied but they have not proven to be as satisfactory as Strain 19.²⁶

Occasionally calves or cows show generalized reactions for up to 7 days after vaccination with Strain 19 including, elevated temperatures, rapid respiration, dullness and anorexia. In rare instances, deaths of calves due to anaphylaxis or *Brucella* septicemia may occur within a few hours or several days.³⁵ Bull calves or adult bulls should not be vaccinated as Strain 19 may rarely localize in their genital tract and a persistent serum titer may develop. No useful purpose, other than providing a degree of immunity, is achieved by the vaccination of male cattle. Veterinarians should use great care that contaminated syringes used for vaccinating calves with Strain 19 are not used for other injections as brucella-infection and serum titers can be produced in other cattle in this manner.³

Recent studies have shown that a reduced dose of Strain 19 vaccine containing about 1 to 3×10^9 *Br. abortus* organisms, instead of the former recommended dose of about 25 to 125×10^9 organisms, given subcutaneously to calves, yearlings or adults resulted in fewer, less severe reactions to the vaccine. But high levels of immunity, up to 80 to 90 percent on a herd basis, were produced. Abortifacient effects of Strain 19 vaccination with the former large or reduced doses are minimal and uncommon in cows vaccinated during gestation. The reduced-dose of Strain 19 vaccine also greatly decreased the number of persistent udder infections when compared to the former massive dose.^{2,27} Even cattle vaccinated with very small doses subcutaneously or conjunctivally became immune.^{8,23,24,20,27,30,31} Furthermore the reduced subcutaneous doses of vaccine, $1/25$ th the former dose, have resulted in no decrease in protection when compared to the former standard dose and significantly decreased the length of time post-vaccinal titers persisted. However, in adult vaccinated herds supplemental serologic tests, especially complement fixation and rivanol tests, are necessary to reduce or minimize false positive serologic reactions with sensitive procedures such as the standard agglutination tube or card tests when done within 2 to 4 months of vaccination.^{2,24,26} Owners of herds in the acute infection phase of brucel-

losis at the time of adult vaccination should expect occasional abortions to continue, usually with a marked reduction after 60 days. In chronically infected herds adult vaccination will produce little immediate change in clinical signs of the disease. With proper management of infected herds most adult vaccinated herds can be free of brucellosis within 2 or 3 years.^{2,26} Non-vaccinated heifers or cows should not be introduced into these acutely or chronically infected herds or areas as they are highly susceptible to *Br. abortus* infection and may cause an increased incidence of infection and prolong the eventual control or eradication of the disease.^{38,39}

After vaccination of large numbers of calves in an area has continued for 4 to 8 years, various test and eradication programs can be instituted until the area is free of brucellosis resulting in minimal losses to the farmers.

The milk ring test (MRT) is an efficient method for the surveillance of possible brucellosis in dairy herds. The market cattle test or "back tag" method is used for beef herds but is less efficient and effective than the MRT. Blood samples are collected on cattle at auction sales and abattoirs and, if positive, the herd of origin is tested. The use of supplemental serologic tests combined with bacteriologic findings have given excellent results in eliminating infection in problem herds.^{26,28} In some herds the MRT is positive but there are no reactors to tube or plate agglutination tests. Supplemental procedures are also useful in these herds.

Over the past 45 years the incidence of brucellosis in cattle in the United States has been reduced from about 10 to 15 percent to about 0.5 to 1.0 percent with a marked reduction in human cases of brucellosis. This has been accomplished by official federal and state brucellosis control and eradication programs with the cooperation and support of cattle owners and veterinarians at a cost of over 2 billion dollars. However eradication of brucellosis is still a distant goal.

Presently there are 10 states, mostly in the southern part of United States, each with 300 to 3,000 known infected herds, that comprise 90 percent of the infected herds. In spite of greatly increased control activities and expenditures, the percentage and numbers of blood test reactors have not decreased in the past 20 years. There are a number of obvious and significant factors that mitigate against a prompt conclusion to a brucellosis eradication program:

(1) The intrinsic nature of the disease has been further elucidated by the coordination of older and more recent studies. Brucellosis is an insidious disease with both latent and acute manifestations, with a variable and often prolonged incubation period. In the absence of practical diagnostic cultural methods to detect carrier animals, a

somewhat confusing, inconsistent and often apparently arbitrary serologic tests and their interpretation have been relied upon.

(2) The changing aspects of the cattle industry in recent years has been toward much larger dairy herds of 200 to 2,000 head of cattle with confinement housing. Beef herds, especially in the southern part of the United States where stock is pastured the year around, have also greatly increased in size. Along with this increased size of cattle herds, the mobility of cattle and the need for many replacement cattle provided by truck transport from other cattle-raising areas has greatly increased. Thus, the opportunity for within herd spread of disease that is very difficult or impossible to control in large units is made more certain by the introduction of infected animals from other herds or areas. In 1978 about 2,000 herds in the United States were "depopulated" at a great cost because brucellosis could not be controlled in them by routine procedures.¹²

(3) Miscellaneous obstacles to an eradication program are the facts that brucellosis may occasionally be carried by many other domestic animals and some wild animals.²⁰ The costs of an eradication program are escalating to the point of diminishing returns. Although in recent years the Federal and State brucellosis control and eradication program has become somewhat more flexible, it is still a fairly rigid, restrictive program that is not highly acceptable to many individual cattle owners and veterinarians. Furthermore because of the complexities and severity of the disease, especially in large purebred herds, the vagaries of serologic testing and the rigidity of the state and federal regulations which are often political and don't always conform to the actual nature of the disease, brucellosis testing has a high malpractice potential for the veterinarian and the owner selling cattle.³⁶ A continuous long term country-wide vaccination program of calves and, if necessary, adult cattle is essential along with other proven control measures.

"Future efforts should be directed toward a broad-based control program which emphasizes prevention and is founded on solid scientific economic and logistic standards."²⁵ If this is accomplished the goal of eventual eradication of brucellosis in the United States might be a possibility.

Leptospirosis is due to small filamentous spirochetes with about 150 serotypes in 18 serogroups.¹¹ The six serotypes most commonly infectious for cattle are *Leptospira pomona*, *L. hardjo*, *L. grippityphosa*, *L. canicola*, *L. icterohemorrhagiae* and *L. szwajizak*. In the U.S. *L. pomona* and *L. hardjo* are the most common and serious of the six as a cause of disease and abortion in cattle.^{11,10,21} *L. sejroe* was also isolated from

the kidneys of aborting cows and serologic evidence of the infection was confirmatory in an outbreak of leptospirosis in cattle characterized by abortion, stillbirth and weak calves.¹³ The incidence of leptospiral antibodies in serum of cattle in the United States varies from 5 to 20 percent in random herds to 50 percent or more in herds and animals suspected of having leptospirosis.^{5,10,11} Leptospirosis is not amenable to eradication because of the widespread occurrence of the serotypes in many species of wild and domestic animals and because of the difficulties in detecting carrier animals. *Leptospira* are found in all species of domestic animals including dogs and cats but are most widespread in swine and cattle. Swine may shed organisms in the urine for six months to a year or more. Some of the wild animals found to shed leptospira in the urine include: skunks, raccoons, opossums, foxes, wild cats, beavers, nutria, rabbits, woodchucks, moles, shrews, mice, rats, deer and others.¹¹ The first three animals have the highest incidence of infection and the skunk, like the pig, can shed organisms for a year or longer. However with *L. hardjo* evidence indicates that the bovine animal is the major, or possibly the only, maintenance host^{5b} and can shed the organism for more than one year.^{10b} Man can become infected with various leptospira but more than half of the human cases in the U.S. due to *L. pomona* has been caused by swimming in contaminated surface water or has occurred in abattoir or dairy workers, especially the latter working in milking parlors with sunken walkways resulting in a exposure to bovine urine.^{3,9} These organisms are readily destroyed by heat, sunlight, drying, acid, and chemical disinfectants. They can survive for days or weeks in a moist environment at moderate temperatures as in stagnant ponds, streams or wet soil.

Leptospirosis was first described in cattle in the U.S. in 1944 and 1948.^{1,12} Subsequent work has shown the disease to be widespread in cattle in the U.S. as it is in most other countries of the world. Outbreaks of the disease in cattle herds may be rather sporadic. The incidence of herd epizootics varies from year to year and may be more common in certain geographical areas. *Leptospira* enter the cow by penetration of the abraded skin of the feet and legs when wading and by passage through the mucous membranes of the mouth and pharynx, nose and eyes by contact with contaminated water and feed or urine. Bulls infected with *L. pomona* shed the organisms in their semen and urine for months or more and could infect susceptible cows by natural service.¹⁷ *L. pomona* can survive for 7 days at 5° C in standard bovine semen extender containing 500 units of penicillin and 500 micrograms of streptomycin per ml. It was later shown that the addition of penicillin (1000

units) and streptomycin (1000 micrograms) per ml. of extended semen prevented the transmission of *L. pomona* in extended frozen semen because of the combined effects of dilution, antibiotic action and chilling on the organism.² However, in artificial insemination studs only bulls free from leptospirosis should be used.^{3,16}

The incubation period in cattle is 4 to 10 days when an elevation of body temperature to 103 to 107° F occurs together with a leptospiremia that lasts for 2 to 6 days. The signs of the acute disease may vary from mild or inapparent signs in about 70 percent or more of affected cows, to moderate signs with anorexia, a drop in milk flow with a slack udder containing slightly thick, "gargety" colostrum-like milk in about 25 to 30 percent of the cases in dairy cattle, to severe signs in a few cattle with a marked drop in milk with a thick secretion containing blood clots, a flaccid udder, severe loss of appetite and loss of condition, anemia, hemoglobinuria, dyspnea, icterus and rarely death within one to three days. The severe cases are seen more frequently in young cattle up to 8 months of age. In rare cases neurologic manifestations due to leptospiral meningitis in young cattle have been reported.^{4,10} Following recovery from the acute period of illness the leptospira tend to localize in the tubules of the bovine kidney and organisms are shed in the urine in variable numbers for 2 to 3 months and occasionally up to 1 year or more.^{5a,5b,23a} Leptospira may also be shed in the milk during the acute stage of illness. A serologic response can usually be elicited within one week after exposure to leptospira and the serum titer usually reaches a peak in about 2 to 6 weeks and then declines to more moderate levels but persists in many cattle for 5 or more years.^{5,6,15} After intravenous inoculations of heifers with *L. pomona* organisms between 150 and 180 days of gestation, abortions occurred 18 to 19 days later. In 5 heifers dead fetuses were present in heifers 17 days after inoculation. No *L. pomona* organisms were present in the blood after the 6th day and antibody titers of 1/100 to 1/1,000 were present on the tenth day. No organisms were recovered from the fetuses apparently due to autolytic changes.¹⁴

In all forms of the disease abortions, especially in cows in the last half of gestation, may occur from 1 to 4 weeks after the acute febrile or leptospiremic stage in *L. pomona* infections^{5,6,10,19} and from 6 to 12 weeks in *L. hardjo* infections. Thus serologic titers should be high at the time of abortion in the former infection and falling or low in the latter.^{5c} The incidence of abortion may vary from 5 to 40 percent of the herd depending upon the number of susceptible cattle in the last third of gestation, the numbers and virulence of the infective organisms and the opportunity for the spread of the infection. Not all

susceptible infected cows in advanced pregnancy will abort. Occasionally an infected cow will give birth to a live, weak, infected calf that dies within a few days. Retained placenta and its sequelae of metritis and infertility are common. Recovered animals are immune to the leptospiral serotype causing the illness and abortion but are still susceptible to infection with other serotypes.^{10,21}

Abortion outbreaks are seen most often in susceptible cattle during the pasture season. The disease can be introduced into a herd by purchasing an infected cow, from cows infected at fairs or shows, from swine running with cattle or from contact with infected wildlife. In range herds serious outbreaks have followed the concentration of stock for winter feeding, blood testing, vaccination, dipping, worming or pregnancy examinations, or other situations where the spread of the urinary infection is favored.^{4,10}

Fetal death and abortion has been shown to be the usual consequence of an acute or subacute fetal infection.^{7,8} The time of 2 to 5 weeks from the initial infection of the cow with *L. pomona* and abortion is the time required for the two consecutive infections in the dam and fetus to complete their courses. Organisms can be demonstrated on silver-impregnated stained sections of fetal livers and kidneys. Organisms are seldom isolated from aborted fetuses because they fail to survive the 12 to 48 hours between the death of the fetus and abortion and the autolysis that occurs in the decomposing fetal tissues. Autolytic lesions characteristic of abortions due to a variety of causes in the cow may be observed in the fetus and fetal membranes but gross diagnostic lesions are not present.

The diagnosis of abortions due to leptospira in cattle is more difficult than those due to brucellosis. The history and clinical symptoms as described above, together with necropsy findings of widespread petechia indicative of a severe septicemia are helpful. Culture of the fetus, especially the kidney, for leptospira in laboratory animals or in special media is difficult and requires time, skill and experience.^{5c} Silver staining of liver and kidney sections may be helpful if autolysis is not severe. Dark-field examination of material from fresh aborted fetuses or urine may reveal the leptospiral organisms with their typical "spinning" motion.¹⁰ The use of the fluorescent antibody technique with a carefully prepared conjugate from an organism from a fetus on tissue homogenates of lung, liver or kidney of aborted fetuses have proven quite accurate even when autolysis was severe.^{5c,18} The fluorescent antibody technique may also be used to stain leptospire in infected urine from aborting cows; culturing of urine at this time may also be diagnostic.

Serologic tests for the diagnosis of leptospiral abortion

have a number of shortcomings. By the time the cow is infected and has a leptospiremia that affects the fetus resulting in its death and abortion, the cow is serologically positive. Because this serologic reaction can persist for years the time of exposure cannot be determined. However a high titer may be indicative of a fairly recent infection. Generally there is little relationship between antibody levels and abortion.^{4,5,6,10,23a} Blood samples taken at the time of abortion and then several weeks later often are not diagnostic.^{10,21} Taking at least 10 blood samples at random from the herd in which leptospiral abortion is suspected including some from cows that have aborted, as well as from nonaborting cows is more diagnostic.²¹ If recently aborting cows have a high titer and nonaborting cows generally have negative titers a diagnosis may be warranted; but if some of the cows that recently aborted are positive only in a low titer a definite diagnosis of leptospirosis is not justified.

Ellis has reported on *L. hardjo* infection of cattle in Northern Ireland where 4 to 6 percent of aborted fetuses and 68.7 percent of aborted fetuses from herds with abortion problems were positive based on culture, immunofluorescence and fetal serology. Only 4.6 percent of abattoir collected fetuses were positive for *L. hardjo* based on culture and fluorescent tests and these fetuses were negative on serologic tests. Using the microscopic agglutination (MA) test, which was superior to the CF and plate test, with a fairly sensitive antigen since serologic titers with *L. hardjo* are definitely lower than those of *L. pomona*, 81.2 percent of aborting cows with a titer of 1:1000 or more had *L. hardjo*-infected fetuses but these comprised only 46.3 percent of aborting cows with *L. hardjo*-infected fetuses. Of aborting cows with *L. hardjo*-infected fetuses 22.8 percent had no detectable antibodies. Paired serum samples have little or no diagnostic value since serologic titers are declining at the time of abortion due to *L. hardjo*.^{5c,d,e} In *L. pomona* abortions, because they occur more acutely, paired samples may be of some value.

Two serologic tests have been adopted and used by various diagnostic laboratories. They are the macroscopic plate agglutination test using many serogroup formalin-killed leptospiral antigens, and the microscopic agglutination test with live antigens. Agglutination in the 1:40 dilution or greater is considered positive with the macroscopic plate test. Some workers consider agglutination at a 1:10 dilution significant with *L. hardjo*. Agglutination in the 1:100 dilution or greater is considered positive with the microscopic agglutination (MA) test.¹⁰ Other special serologic tests have been used but have not been generally adopted. Vaccinated cattle will have a serologic titer for many months.

Since eradication of leptospirosis is not possible, control and treatment of bovine leptospirosis may be accomplished by hygiene and sanitation, vaccination and antibiotic therapy. Water supplies should be protected from contamination, wet areas should be drained or fenced off, ingestion of contaminated feed should be prevented and exposure to infected urine and semen should be avoided. Newly purchased animals might be serologically tested, isolated and retested in two or three weeks. If these animals are positive, parenteral antibiotic therapy would be indicated before introducing them into the herd. If negative, vaccination would be desirable. Since cattle recovering from leptospirosis are immune from reinfection with that serotype, various vaccines have been developed and evaluated. Multivalent bacterins containing 3 or more serotypes are widely used and provide an excellent immunity for a period of 6 to 12 months. For this reason some cattle subject to frequent possible exposure to leptospirosis are vaccinated twice yearly. If breeding is limited to a short period or infection occurs only during certain seasons of the year, once a year vaccination is usually satisfactory. Vaccination will provide protection against the clinical forms of the disease but it does not provide complete protection against infection and the urinary shedder state.

In the face of a herd outbreak of abortion due to leptospirosis, all cattle, especially pregnant cows should be promptly vaccinated. It may be advisable to give aborting, exposed cows or all the cows 25 mg of dihydrostreptomycin per kg. of body weight intramuscularly to eliminate the carrier or shedder state and reduce the spread of the infection in the herd.^{4,10,19,20,23} Others have administered therapeutic doses of dihydrostreptomycin or tetracyclines for several days. Antibiotic treatment at the same time as vaccine injection does not interfere with the development of immunity.^{10,20} Abortions may continue for several weeks until an immunity from the bacterin is produced. Vaccination of cows in advanced pregnancy provides a degree of colostral immunity for calves that lasts until they are 3 to 4 months of age when vaccination is indicated in areas or on farms with a high incidence of the disease. With the advent of more highly concentrated purified bacterins the incidence of cases of anaphylaxis at vaccination has declined markedly.

The treatment of the acute stages of leptospirosis includes the parenteral administration of large doses of antibiotics including dihydrostreptomycin 5 gms, twice daily, or the tetracyclines, 2.5 to 5 gms, daily, per 1,000 lb. animal for 5 days. This treatment also eliminates the renal carrier state. Early treatment is essential^{10,20} to possibly prevent death or abortion. Guidelines for the prevention and control of leptospirosis in bull studs has been out-

lined including serologic, vaccination and treatment procedures.²² In cases with hemoglobinuria and anemia, blood transfusions and supportive therapy may also be indicated but the prognosis in severe cases is poor.^{4,9}

Campylobacteriosis (Vibriosis) due to **Campylobacter fetus venerealis** is an occasional cause for a 2 to 10 percent incidence of abortion in susceptible herds. Vibriosis is a venereal disease that can be transmitted at coitus. Older bulls may be chronically infected. The organism may be present and infective in improperly treated semen. With widespread artificial insemination using antibiotic-treated semen, abortions due to **C. fetus** are presently uncommon in dairy areas. Occasional sporadic abortions due to **C. fetus intestinalis** occur the third trimester of gestation in cattle. Because vibriosis in cattle is more closely associated with infertility and early embryonic deaths than abortion this disease will be discussed in Chapter XIII on Infertility in Cattle.

Listeriosis is caused by **Listeria monocytogenes** which is a gram-positive slightly motile rod or coccoid organism with a wide host range among mammals and birds throughout the world. Although infection with *Listeria* is frequent, the occurrence of clinical disease is uncommon. Numerous antigenic serotypes are recognized. **L. monocytogenes** is widespread in nature and is resistant to adverse environmental factors as it can be found in moist or dry soil, bedding, fecal material and secretions and tissues of normal and diseased animals. It has been found in silage and actually propagates in poor quality silage with a high pH.^{4,11,2,3,5} The organisms can penetrate the intact mucous membrane of the respiratory or alimentary tracts producing a transient rise in body temperature due to a bacteremia. A latent infection in various organs may then be established although clinical signs are uncommon and these carrier animals may spread the organism for a long period in their nasal secretions and feces. Sudden changes in management or feeding practices inducing stress and lowered resistance are often associated with outbreaks of clinical cases of listeriosis. A close relationship between silage feeding and the incidence of this disease is frequently observed. Listeriosis is observed more often in the late winter and spring months. The incidence varies greatly between years.

Three clinical forms of listeriosis are observed: **the septicemic form** affecting young perinatal animals and humans and characterized by the early death of the newborn with hepatic lesions, gastroenteritis and meningitis,⁶ **the encephalitic form** affecting relatively mature animals, especially ruminants with meningoencephalitis; and **the reproductive form**, seen in ruminants and humans, characterized by abortion the last trimester of gestation without clinical illness. *Listeria* organisms are car-

ried hematogenously to the placenta and into the amniotic fluid and fetus.^{4,3} The above forms may be observed together in the same outbreak. In cattle aborting from the 7th to 9th month of gestation the fetus may be well-preserved with few if any lesions in the fetal organs. Retained placenta, metritis and dystocia were commonly observed. If fetal death occurred before the 7th month the fetus was often retained **in utero** for up to 5 days before expulsion, autolysis of the fetus was advanced and retained placenta and metritis were not uncommon.^{11,12} In women infection due to *Listeria* apparently persists and may result in habitual abortion.^{1,3,10} Recurrent bovine listeric abortions may recur each year on some farms and even in the same animal.^{3,9}

Sporadic bovine abortions due to *Listeria* are seen most frequently but occasionally herd outbreaks may occur with a 5 to 15 percent, and rarely higher, incidence.^{9,11,12} Fetuses are usually expelled dead but a few calves may be weak at birth and die shortly thereafter. A history of the introduction of carrier animals from affected herds, or a recent change to silage feeding, or some severe stress may be associated with an outbreak. *Listeria* were isolated from the feces in 25 percent and from the milk in 16 percent of cows aborting due to listeriosis.^{3b} The healthy carrier animal may be a latent and important reservoir of infection. *Listeria* infection may pass between different species. There are no suggestive or pathognomonic lesions of listeriosis in aborted fetuses and membranes other than occasional small focal, necrotic areas in the liver. The diagnosis is based on the isolation and identification of the organism which may be difficult.

Fetuses should be collected, chilled and cultured promptly. Taking a large volume of tissue from the fetus, preferably the liver and thoroughly macerating and emulsifying it in a nutrient broth is advised. After inoculating bacteriologic media, the emulsion should be stored at 4° C. and recultured repeatedly especially if listeriosis is suspected.^{9,11} This latter procedure is important for the recovery of ***Listeria monocytogenes***. In most cases the organism was recovered on reculture within 20 days of storage but sometimes recovery occurred only after 6 months of storage. A rapid method for the isolation of *Listeria* by inoculating 20 day old mice intracerebrally with suspect material was described.⁷ This cold enrichment method is not as necessary for culturing fetal body tissues as it is for brain tissue.¹⁷ *Listeria* were usually recovered from the exudate in the genital tract taken shortly after abortion, the placentomes, the spleen, the brain, the stomach and the kidneys of aborted fetuses.^{8,9} In fetuses that have undergone little autolysis small pinpoint yellow foci of necrosis may be observed in the liver and spleen.^{15,8,9} In experimental aborting cattle, *Listeria*

were recovered from the genital tract for about 10 days after abortion, and from body tissues at slaughter 25 to 36 days after abortion.⁸ The immunofluorescent methods for the detection of *Listeria* in fetal tissues are of diagnostic value in cattle.^{11,3b}

A rise in the agglutinin titer in affected animals based on the somatic agglutination tests conducted on blood samples taken at the time of abortion and 60 to 90 days later, and on the basis of the antigen-fixation test was reported.^{8,9} They showed this infection to be widespread in animals in affected herds. In the experimental cattle the antibody titers reached a peak at the time of abortion and dropped rapidly within the next 30 days. Further work is necessary to develop serologic tests to the stage where they are precise enough for routine diagnostic application.

Therapy or treatment of herds with abortions due to *Listeria* would include the cessation of silage feeding if this was occurring and controlling other factors that might lower the resistance of the cattle. Hygiene and sanitation practices consisting of segregation of aborting cattle and destruction of aborted fetuses and membranes should be followed. Antibiotic therapy with large doses of the tetracyclines or penicillin and streptomycin for four to five days might be attempted in valuable animals. In herds where the disease tends to recur the use of an autogenous bacterin might prove of value.⁴ No commercial bacterin is available.

Salmonellosis in cattle is principally caused by *S. typhimurium* and *S. dublin* with occasional outbreaks caused by other serotypes.^{4,11,5,6,7} *S. typhimurium* is widespread in the world in many species of animals and feed. *S. dublin* is host adapted to cattle and occurs in Europe, Great Britain and western United States. In recent years evidence has indicated the latter serotype is spreading eastward and in the future will probably be of concern to veterinarians throughout the United States.¹ *S. dublin* is highly contagious for humans. Carrier cattle commonly occur in *S. dublin*-infected animals as the organism often colonizes in the gall bladder and is spread in the feces for years or a lifetime. Whereas cattle infected with *S. typhimurium* usually only remain carriers and shedders for several months.^{11,5,6} Herds can be freed of *S. dublin* infection by culturing fecal samples of all cattle in the herd and eliminating all infected cattle.

Abortion is only sporadic in pregnant cows with clinical signs of *S. typhimurium* infection. Abortion is usually caused by infection of the fetus and its membranes with fetal death or possibly it may be secondary to the hyperthermia and stress of the acute severe enteritis and septicemia in the pregnant cow. Abortions occur in the

second half of the gestation period and usually within 10 to 20 days of the onset of the clinical disease in the pregnant cow. *S. typhimurium* can usually be recovered from the feces of the cow and the autolysed fetus.^{4,11,4,6}

Abortion due to *S. dublin* however frequently produces abortion after midgestation without clinical signs of enteritis and septicemia in the cow. *Salmonella dublin* abortion was clinically seen as only abortion in 77 percent of the cases. It was associated with enteritis in 14 percent of the cases and in most of these abortion followed the dysentery. In most *S. dublin* abortions, not accompanied by diarrhea, the infection present in the feces, vaginal mucus and milk ceased 3 to 5 weeks after the abortion. Adult cattle recovering from *S. dublin* dysentery invariably became consistent fecal excretors of the organism and this was associated with congenital infection of some of the calves at subsequent calvings.³ *S. dublin* can be readily recovered by culture from the aborted fetus and fetal membranes and from genital discharges for 3 to 5 weeks after the abortion. The mortality in cows infected with *S. typhimurium* is higher than in cows with *S. dublin*.^{11,6,7}

In both types of salmonella infections stress produced by a change in feed, shipping, surgical operations or acute illness may result in releasing latent or quiescent infections that can cause an epizootic outbreak in susceptible cattle.^{2,4,5} Following salmonella abortion retained placentas and metritis are common but most cows recover and subsequently conceive. Veterinarians handling abortions and their sequelae should take precautions to protect themselves from infection. Treatment with antibiotics usually does not prevent the carrier state so affected animals particularly those carrying *S. dublin* should be isolated and after recovery consideration should be given for their slaughter in an effort to eliminate infection in the herd. Vaccines, both live and dead, for both above serotypes, are available in Great Britain but their value is difficult to assess.^{4,5a,7} In other countries an autogenous bacterin might be considered under certain circumstances especially to protect newborn calves by immunization of the dam prior to birth so colostral antibodies are high. Vaccines, however, cannot substitute for good management and hygiene in the control of salmonellosis.^{5a,7}

Miscellaneous Bacteria and Organisms, Not Including Fungi, Viruses or Protozoa.

Tuberculosis caused by *Mycobacterium bovis* is present worldwide in cattle and is of major importance in dairy cattle that are closely housed or pastured in limited areas. In the past 30 years tuberculosis in cattle has been reduced to a very low level in the U.S. and out-

breaks of tuberculosis, particularly advanced cases in which the genital organs may be involved are extremely rare. In other countries where tuberculosis is still common it may occasionally cause metritis, salpingitis, infertility and recurring abortion. Abortion in cattle due to *M. avium* has been described.^{6,29} Tuberculosis due to *M. bovis* may also occur in man, goats, pigs, deer and occasionally other wild animals. The infected animal may spread the disease organisms in excreted air, sputum, feces, milk, urine, semen and genital tract discharges. Susceptible animals either ingest or inhale the infective organisms. Moisture favors the survival of the organism for long periods outside the body.^{4,11} Occasionally cows may become infected at coitus with a bull with lesions of the prepuce and penis, accessory glands or testes,⁴¹ or by intrauterine insemination of infective semen.^{3,31} The bull may on occasions be only a carrier or contact spreader between an infected cow with a tubercular genital discharge and a susceptible cow. Uterine tuberculosis however is uncommon but may result from, coitus with an infected bull, intrauterine insemination with infective semen, by continuity from peritoneal tuberculosis, or probably most often by hematogenous spread. In tuberculous metritis infertility is frequent and recurrent abortion or the birth of a tubercular calf that dies a short while later may occur. Retained placenta and lesions in the placenta similar to those of brucellosis may occur and a chronic "curdled milk" type of uterine exudate that persists is often observed in this form of tuberculosis.^{4,11} The bilateral granulomatous uterine lesions, salpingitis and adhesions may be palpated per rectum in the non-pregnant cow or cow in early pregnancy.

Infected animals should be eliminated and the disease eradicated in the herd and geographical area if possible. The intradermal tuberculin test applied regularly with the removal and slaughter of reactors has been used quite successfully in the U.S. to greatly reduce the incidence of the disease. False positive reactions to this test may occur due to other mycobacteria. In cases of uterine tuberculosis the disease may be so advanced that no reaction will be elicited on the intradermal tuberculin test.⁴¹ In isolated cases of uterine infections, culture of the fetus, the fetal membranes and the genital discharges usually reveal the organism. If cases of this type are present in a herd usually other cases of generalized pulmonary or intestinal types are present also. Further information on bovine tuberculosis, diagnostic tests, control measures and vaccination are reviewed elsewhere.^{4,11}

Miscellaneous bacterial infections associated with sporadic bovine abortions include the so-called "wound" infection organisms that are probably carried to the pregnant uterus by the blood stream or possibly by extension

from the caudal portions of the genital tract.³⁰ These organisms probably originate in infectious processes such as: traumatic gastritis, liver abscesses, ulcers of the stomach or intestine, abscesses in the lung, foot rot, acute mastitis, and pneumonia. These organisms include: *Bacillus* spp.; streptococci; diplococci;⁴⁰ staphylococci; *E. coli*, *Alcaligenes fecalis*; *Pseudomonas aeruginosa*; *Corynebacterium pyogenes*, *Erysipelothrix insidiosa*; *Bacillus cereus*, which causes a necrotizing placentitis;⁴⁴ *Yersinia pseudotuberculosis*;²⁰ *Serratia marcescens*;^{18,43} *Hemophilus somnus*;¹¹ and *Spherophorus necrophorus*.⁴⁰ *Vibrio fetus intestinalis*, a common cause of abortion in sheep, only occasionally causes sporadic abortion in cattle.¹⁵ *Mycobacterium avium* has been reported as a cause of sporadic abortions in cattle that are housed with infected chickens. In this latter disease small granulomatous lesions develop in the endometrium and placenta and recurrent abortions may occur as with *M. bovis*.^{6,29}

Sporadic abortions are infrequently associated with febrile septicemic bovine diseases such as pasteurellosis due to *Pasteurella multocida*,^{18,40} actinomycetes (*Northcardia asteroides*) and anthrax. *Mycoplasma bovis* and *M. agalactiae* var. *bovis*,^{3,10b,16c,20b,32} have been recovered from aborted bovine fetuses.^{20,1,2,3,8,32} *Mycoplasma* and *ureaplasma* have been found in the fetal membranes and fetuses of spontaneous abortions in women.^{13,19} *Ureaplasma* have been isolated from aborted bovine fetuses.^{10c,20b} To illustrate the ability of a variety of organisms to cause abortion in cattle by the hematogenous route, the author observed a pregnant cow given *Streptococcus agalactiae*, an organism not considered pathogenic outside the bovine udder, intravenously. Ten days later the cow aborted and a pure culture of the organism was recovered from the fetal organs. If mixed cultures of organisms are obtained from the aborted fetus the possibility of contamination of the fetus following death, or during expulsion, should be considered.

Endotoxin produced by gram-negative organisms can cause abortions in cows, ewes, sows and does.^{5,10} It was proposed that endotoxins and the associated severe stress reactions were the cause of some abortions in animals rather than the elevated body temperatures that frequently accompany septicemic and toxic infections with gram-negative organisms.^{7,10}

***Hemophilus somnus* (agni)** the wide spread causative agent of the sporadic diseases of bovine thromboembolic meningoencephalitis and pneumonia, especially in feeder cattle has been reported as a cause of abortion and possibly infertility.^{18,20b,39}

Rickettsial infections of *Coxiella burnetii* caused Q fever worldwide and *Ehrlichia* (*Rickettsia*) *phagocy-*

tophilia causing tick-borne fever in Great Britain and Europe have been reported as causing bovine abortion.^{4,12,42} **Coxiella burnetii** occurs mainly in dairy cattle in areas of the United States and world-wide. Cattle are one of the major hosts shedding large numbers of organisms, that are infectious for man, at successive parturitions in the placenta, its fluids and milk. Between calving periods the infection may remain latent.⁴ Abortions due to **Coxiella burnetii** have been produced in cattle experimentally but in naturally infected cows abortions are rare.^{4,11,12} In tick-borne fever in cattle abortions, which occur the last two months of gestation, follow a period of pyrexia. It is not known whether abortions are due to the fever and stress or to the rickettsial organism.^{4,11}

Epizootic Bovine Abortion (E.B.A.) or foothill abortion is apparently caused by an agent of the psittacosis lymphogranuloma, **Chlamydia psittaci**, group of organisms, an obligate intracellular pathogen.^{4,11,20,23,25,34,36} In 1956 this disease that had been observed in California since 1923 was called epizootic bovine abortion (E.B.A.).¹⁴ Because of breeding practices in beef herds it occurred mostly in first calf heifers or newly introduced cattle during the months of July through October in the foothills adjacent to the Sacramento and San Joaquin valleys. Fetuses were expelled during the 6th to 8th months of gestation. The incidence of abortion would reach 30 to 40 percent in some herds with occasionally up to 75 percent or more of susceptible females aborting. In a susceptible herd animals of all ages would abort but thereafter abortion was largely limited to heifers. Recent studies on the nature of EBA or foothill abortion have indicated a tick, **Ornithodoros coriaceus** is the probable vector of the causative agent. These ticks harbor **Chlamydia** and two different viruses. The latter were found not to cause

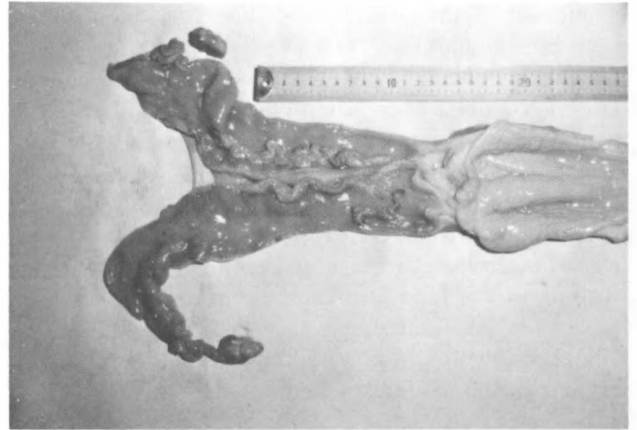


Figure 60. Bovine fetal resorption 60 days post-conception.

abortion.²⁶ However this tick has been shown to harbor the IBR virus. (See viral abortions.) **Chlamydia** abortions have been reported in the Intermountain region in both the epizootic and sporadic forms and to occur in February and March in beef herds and throughout the year in dairy herds. McEntee and coworkers in New York State have tentatively diagnosed rare sporadic cases of this type of abortion in dairy cattle from its characteristic lesions although the causative agent has not been isolated.^{20,22,20b} The disease has been described in central and southern Europe.³⁶ Since typical lesions of chlamydial abortion have been described in areas where neither ticks nor a typical pattern of EBA abortion occurs and since two capable researchers in California question whether EBA or foothill abortion is caused only by **Chlamydia**^{15,15,16,17} this author reserves judgement until further study resolves the etiologic factors involved. There is definite evidence from experimental and clinical studies that **Chlamydia** can cause abortion when injected into susceptible pregnant cows. Further studies are needed in cattle to demonstrate whether intestinal chlamydial infections can be transmitted by the oral route as occurs in sheep and other species. Great similarities exist between EBA and enzootic abortion of ewes (EAE) which is due to the same, or very similar chlamydial agent.^{23,36} This agent has also been isolated from bulls affected with a seminal vesiculitis syndrome.³⁵ Mycoplasma infection of the male bovine genital tract can simulate this syndrome. Thus the present name of the disease may be a misnomer because it is not limited to epizootic outbreaks and it may cause abortion and possibly other disease syndromes in both cattle and sheep.

Outbreaks of E.B.A. occur suddenly without premonitory signs of illness or impending abortion. The disease primarily affects the fetus as there is no clinical evidence

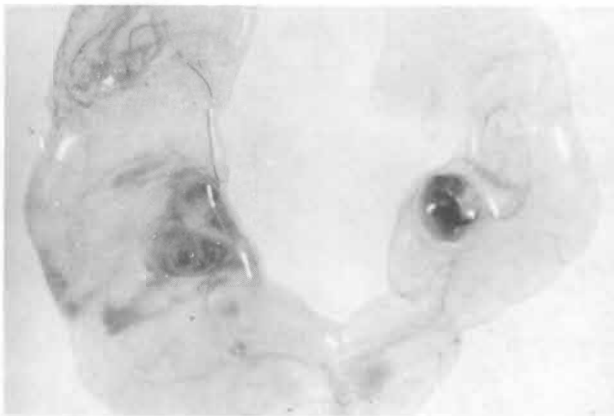


Figure 59. Embryonic death of one of twin 35-day bovine zygotes.

of infection in the cow. Intravenous inoculation of the agent causes abortion 3 to 6 weeks later, intramuscular inoculation 3 months later and subcutaneous inoculation 4 to 4-1/2 months later. Abortions occur from the fourth month of gestation to term but most commonly the 7th, 8th, and 9th months. Some fetuses were expelled dead at term or calves were born alive and weak and succumbed later. About 50 percent of aborting cows had retained placentae and the subsequent fertility of the cows was impaired at least for a number of months.^{23,34} Once a cow aborted an immunity was apparently produced and only occasionally did cows abort a second time due to this agent. Aborted fetuses were clean, fresh and pale or anemic and death had apparently occurred during delivery or shortly thereafter.^{15,15,17} Since fresh fetuses with no autolysis are seen in relatively few forms of abortion in animals for example E.B.A. in cattle and equine herpesvirus 1 in horses, the author would speculate that the adrenals of these fetuses might be hyperplastic thus causing the onset of parturition or abortion prior to the death of the fetus. (See section on hormonal causes of abortion.)

Aborted fetuses exhibited characteristic lesions of anemia and extensive petechial hemorrhages of the conjunctival and oral mucosa and skin. The subcutaneous tissues were edematous especially those of the head. Straw-colored fluid was usually present in the body cavities. The most striking lesion seen in 50 to 60 percent of E.B.A. abortions is the swollen coarsely nodular yellow-colored liver that develops secondary to chronic vascular lesions and chronic passive congestion. (See Figure 62.) Nearly all the lymph glands were enlarged and edematous. The basic histological change of this disease was a granulomatous inflammatory process or a diffuse or focal reticulo-endothelial hyperplasia that irregularly involved all organs. Fetuses aborted before the 7th month are more autolyzed and usually do not have the above typical lesions. The fetal membranes in cases of E.B.A. abortion are usually edematous but are not of diagnostic value.

The recovery of the chlamydial agent from aborted bovine fetuses is more difficult than from aborted ovine fetuses probably because of fewer organisms present due to the chronic disease process in the bovine fetus together with the generalized reaction present indicative of an active defense response. Cultures into the yolk sacs of chicken embryos and in recent years, tissue cultures^{20b} should be made from any or all organs and the placenta and even then many fetuses yield negative results. If the fetus is positive the organism is usually recovered from only one or two organs. The E.B.A. and E.A.E. agents have similar biological and pathogenic properties and share

common specific antigens. Pregnant cows aborted after being inoculated with E.A.E. agent and pregnant sheep aborted after inoculation with the E.B.A. agent.³⁴

The modes of transmission, the reservoirs of the agents or other epidemiological aspects of E.B.A., and E.A.E., have not been clarified. The two diseases occur independently and an interchange of infection between cattle and sheep is probably of minor importance. Veneral transmission may possibly play a role in cattle since workers have recovered *Chlamydia* from the semen and epididymis of young bulls with a seminal vesiculitis syndrome.³⁵ However, it has not been proven that the disease can be transmitted by coitus.^{23,25}

At present there is little that can be done to control the disease. Abortion produces an immunity to future natural infection in most animals. However, various vaccines have been tried without success.²⁴ Preventive management procedures to control EBA have been recommended⁷ that either expose sexually mature heifers to a heavy infestation of infected ticks 3 months before breeding or possibly altering the breeding season so exposure occurs late in gestation.

It is evident that further studies on chlamydial abortions and EBA are necessary to develop a logical comprehensive understanding of the etiologic factors, the pathogenesis and the control of this disease complex. More study is needed on the epidemiologic factors involved in the transmission of this disease.

Viral Causes of Abortion in Cattle

Infectious bovine rhinotracheitis ("red nose") and infectious pustular vulvovaginitis (I.B.R.-I.P.V.) vi-

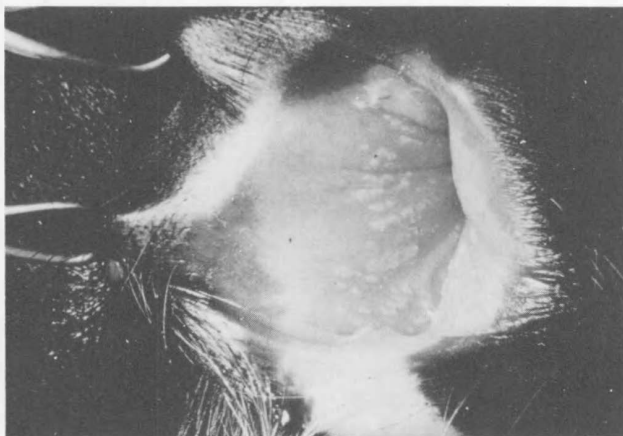


Figure 61. Pustular vulvovaginitis in a heifer due to IBR-IPV virus.

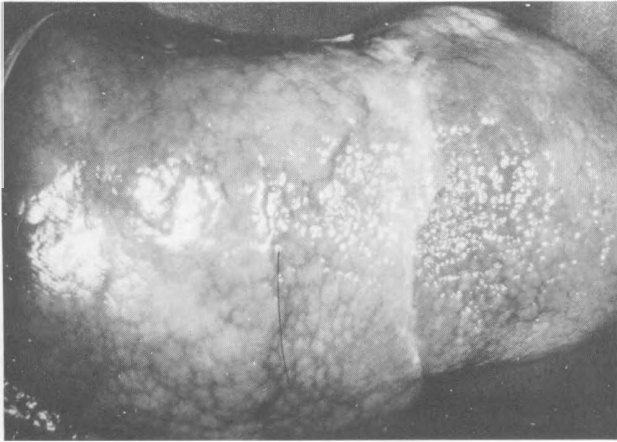


Figure 62. Nodular chronic lesions of the fetal liver in epizootic bovine abortion.

IBR is a common cause of abortion in cattle in the U.S. and in other countries.^{4,13,12} This is a Herpesvirus and has many features similar to rhinopneumonitis virus or equine Herpesvirus 1 in horses, and Herpes simplex in humans. This disease of cattle has received much study over the past 20 years. Other domestic animals are not susceptible to this virus but it has been reported in mule deer.⁴ I.B.R.-I.P.V. virus is widely distributed over the world and in the U.S. The clinical morbidity may vary from 10 to 100 percent in a herd. The mortality is generally under 10 percent with only occasional deaths in adult animals in uncomplicated outbreaks. Deaths in prenatal fetuses and neonatal calves may be high. The diagnosed infectious causes of abortion comprised 23.3 percent of 3812 aborted fetuses examined from 1960 to 1970^{13b} and 34.0 percent of 2500 aborted fetuses examined from 1973 to 1976.¹⁸ Of the diagnosed infectious causes of bovine abortions, IBR comprised 12.6 and 8.8 percent, respectively. Over 90 percent of the diagnosed viral abortions were due to IBR viruses.^{13b,18} Although a generalized viremia develops in nearly all I.B.R.-I.P.V. infections, localized manifestations of the disease occur that confuse the diagnosis.^{4,13,12}

The varied clinical forms of this disease include: (1) The **upper respiratory form** or "red nose" which occurs in cattle feed lots and dairy herds in the Fall and Winter months, and is the most common form seen in the United States and Canada. It is characterized by fever of 104°–107° F., anorexia, depression, reddened nasal mucous membranes and nasal discharge, pustules and ulcers in the mucosa of the nose, pharynx and trachea, infrequent coughing, and a drop in milk production lasting 2 to 7 days except in severe cases in which secondary

tracheitis and pneumonia may occur. (2) The **conjunctival form** which exhibits marked lacrimation changing to a mucopurulent profuse discharge from the eye along with the septicemic signs exhibited in (1). The conjunctiva is reddened and swollen and contains necrotic pustules and ulcers.^{1,27} (3) The **neonatal digestive form** in young calves from birth to 2 to 3 weeks of age is associated with a high mortality and is characterized by severe signs of septicemia resembling that associated with *E. coli* but exhibiting necrotic lesions in the mouth, pharynx, larynx, esophagus and forestomachs with diarrhea and death within 1 to 3 days.³⁴ (4) The **meningoencephalitic form** is seen occasionally in young cattle 4 to 10 months of age and is characterized by dullness, incoordination, tremors, amaurosis, opisthotonus, coma and death within 3 to 4 days.⁷ (5) The **vulvovaginal form**, the most common form of the disease in Europe and Australia,¹⁶ is characterized as in the others by signs of a generalized septicemia but also pustules and ulcers of the vaginal and vulvar mucosa especially in the region of the lymphoid follicles with swelling and a purulent discharge.^{4,16,17} (See Figure 61). This form of the disease was previously called coital vesicular exanthema or Blaschenausschlag. The respiratory form of the disease is rarely observed in outbreaks of this genital form.¹⁵ (6) The **preputial form** in bulls is characterized by pustules and ulceration of the penis and prepuce.³³ IBR in bulls usually causes severe degenerative changes of the seminiferous epithelium and a period of infertility or sterility lasting up to 3 to 4 months. (7) The **prenatal or abortive form** of the disease is characterized by infection and intrauterine death of the fetus and abortion 2 to 5 or more days later.^{16,19} Abortions may occur in all three trimesters of gestation^{16,24} but are most common from midgestation to term. The incidence of abortion in a herd will vary from 5 to over 60 percent with an average of 5 to 20 percent depending on the virulence of the organism and the numbers of susceptible cows in advanced pregnancy.²⁶ Abortions are most common following the respiratory and conjunctival forms²⁷ and rarely occur in cases of infectious pustular vulvovaginitis. Retention of the placenta occurs in about 50 percent of the abortions. (8) The **intrauterine form** of the disease caused a necrotizing endometritis when I.B.R.-I.P.V. virus was present in semen at the time of artificial insemination. This resulted in a tonic, edematous uterus and a short estrous cycle of 9 to 15 days in length. Conception did not occur in 11 of 12 heifers inseminated with semen containing virus but did occur at the next estrus when noninfected semen was used.¹⁸ A herd outbreak of I.B.R.-I.P.V. was reported where strong evidence indicated the infection was introduced by frozen semen shipped from another

state.¹¹ I.B.R.-I.P.V. virus has been recovered from three ampules of frozen semen from a single collection of one bull.³² Frozen semen ampules from 39 other bulls from 3 AI centers were negative for this virus. The author has received a number of reports from veterinarians that a period of infertility lasting about 3 to 4 weeks followed the vaccination of heifers with a live attenuated I.B.R. vaccine.

As noted above all forms are characterized by a viremic and septicemic phase with an elevated temperature, depression, and anorexia lasting from 2 to 10 days but in many animals these signs may be subclinical. In all forms of the disease immunity develops as evidenced by the appearance of virus neutralizing antibodies in the plasma by 14 days after exposure.^{9,12,16} In general if one form appears on a farm the other forms are seldom observed but conjunctivitis is seen occasionally, and meningoencephalitis on rare occasions terminally, with the upper respiratory form. The author has observed a few outbreaks of the upper respiratory form with concurrent vulvovaginal lesions.

Abortions may occur in pregnant animals from 2 weeks to 2 to 3 months^{6,12,16} after any form of the disease, especially the respiratory and conjunctival forms, but is only rarely observed in the vulvovaginal form.

Since abortion is not associated with the genital form of the disease in cattle and since in humans the oral and genital forms of Herpesviruses are serologically distinct, some have speculated that the genital and respiratory forms might also be different in cattle. However, no serological or other differences between viruses recovered from the two sites in cattle could be found.^{2,16} Inoculation of venereal strains of IBR-BVD into the nose and eyes of cattle indicated that these strains were less virulent than the respiratory strains of the virus.^{1b} Recent studies using restriction endonuclease analysis have shown that I.B.R. virus and I.P.V. virus from their respective sites in the body are different even though some similarities were present.^{6b} Further studies are indicated with this IBR-IPV herpesvirus as well as the respiratory and abortive forms of equine herpesvirus 1.

The virus is carried in the blood in the leucocytes and abortions occurred 18 to 64 days after inoculation of the virus.^{10a,23} I.B.R.-I.P.V. virus may cause infection following intranasal, conjunctival, intravaginal, preputial, oral, intrauterine, and intramammary as well as subcutaneous, intramuscular or intravenous inoculation. Besides direct and indirect contact transmission of IBR virus, it may probably be transmitted by arthropod vectors such as *Ornithodoros coriaceus*.^{33b} The site of inoculation determines the clinical form of the disease produced especially in the first four modes of administra-

tion. The incubation period for viremia and the acute manifestations of the disease is 1 to 5 days experimentally and may range from 3 to 10 or 20 days naturally.^{6,19} The I.B.R.-I.P.V. virus in the dam's blood stream during viremia, 2 to 10 days postinoculation, entered the cotyledon but produced no local inflammatory reaction or spread of virus. The viremia terminated in the dam with the development of antibodies detectable in the blood. At the time of abortion the cow has already developed virus neutralizing antibodies in the plasma, therefore paired serum samples taken at the time of abortion and several weeks later are of no diagnostic value. After a week to 2 months the virus, protected from the maternal antibody by its location in the cotyledon, infects the fetus and causes its death within about 24 hours.^{6,16,19} About 50 percent of susceptible animals pregnant 165 days or more, may abort after an IBR viremia whether caused by natural field exposure or by immunization with a modified live virus.¹⁶ In recent years intranasal MLV vaccines have been developed that do not cause abortion in pregnant cows.^{9,12}

Signs of impending abortion are usually not observed. Aborted fetuses are invariably expelled dead with a degree of autolysis. Calves normal at birth may become infected and die in 24 to 48 hours with I.B.R.-I.P.V. viral infection. The lesions described in aborted fetuses may be of diagnostic value. There is no evidence of uterine disease. The placenta shows autolytic nondistinctive lesions characterized by edema and the presence of a yellow, brown amniotic fluid. Autolysis of the fetus is always present to a varying degree with reddish-brown subcutaneous edema and dark red watery fluid in the body cavities. Hemorrhages and petechiae are often widespread in the fetus.

Microscopically characteristic lesions of focal necrosis in the liver, lymph glands, kidneys, other organs and placenta are usually observed.¹⁵ The most striking gross changes occur in the kidneys which are usually surrounded by a marked hemorrhagic edema. A severe hemorrhagic necrosis is confined largely to the cortex and is often so severe that the medulla and part of the cortex are floating in dark red fluid. Pin-point, 1 to 2 mm, necrotic, white foci may be observed in the adrenal glands. Intranuclear inclusion bodies are seen infrequently in these autolysed fetuses,^{16,19,20} but if present are most numerous in the lungs, cotyledons and adrenal glands. During the acute state of illness virus may be recovered from the nasal cavity, the vagina, the conjunctiva and the prepuce in the upper respiratory, the vulvovaginal, the conjunctival and the preputial forms, respectively. Usually within 10 to 26 days after the acute illness the virus disappears.

Culture of the fetal organs and fluids and especially the fetal cotyledon may recover the I.B.R.-I.P.V. virus.^{6,16,24,31} In many cases the virus cannot be recovered because of the advanced autolysis of tissues in the fetus. However, the fetal cotyledon may contain a high level of virus and because of its close proximity to the maternal circulation, autolysis of the fetal placenta and chorion are delayed. I.B.R.-I.P.V. virus has been recovered from a cotyledon following the birth of a normal calf. In bulls the disease may be subclinical and require a number of passages for recovery of the virus and the infection may persist in a latent form for over 360 days. The I.B.R.-I.P.V. virus has been cultured intermittently from the vagina and from the nasal cavity of infected heifers for 578 and 510 days, respectively.^{28,29,31} This prolonged intermittent appearance of the virus even though antibody titers were present in the blood of the animal is characteristic of herpesvirus infections and may explain the frequent reoccurrence of the clinical disease in the field. Many latent herpesviruses will recrudescence when the carrier animal is stressed or when a series of cortisone injections are administered. As with other herpesviruses the site of the latent infection is the trigeminal ganglion cells.⁸

Serological testing using the serum-neutralization test is best conducted on double serum samples taken at the time of the acute illness, when most samples are negative, and again 2 to 6 weeks later. In cases of abortion the serum titers are elevated in the dam at the time of the abortion. In a herd outbreak of I.B.R.-I.P.V., samples might be taken of representative cattle that are normal, recovered, aborting or acutely ill. Samples should be taken in as near sterile a manner as possible in sterile vacuum vials so the serum neutralization test, utilizing tissue cultures will be satisfactory. Antibody response following the various forms of the disease, experimental intravenous or intramuscular inoculations and vaccination is variable.^{9,12,16,23,31} It appears the greatest and most rapid antibody response occurs after abortion and the intravenous and intramuscular administration of virulent I.B.R.-I.P.V. virus. The antibody response is the slowest and poorest after the vulvovaginal and the preputial forms of the disease when the rise in titer may be slow and extend in the latter over 8 months. After vaccination with a number of commercial vaccines some titers did not develop until 4 to 30 months after vaccination. There was evidence that once serum titers developed that fluctuations occurred due to anamnestic responses following recrudescence of virus multiplication but titers remained for at least 3 to 4 years or more or for a lifetime due to the latent infection with the virus. Thus it was evident from serologic studies that I.B.R.-I.P.V. virus acts like

Herpes simplex in humans and rhinopneumonitis virus in horses where clinical lesions with multiplication of the virus may develop even when low levels of antibodies are present in the blood stream. Factors of stress, especially in the winter months, that lower resistance appear favorable for the reappearance of the I.B.R.-I.P.V. virus in body secretions. Massive exposure of mucous membranes to the virus may produce clinical lesions even though antibodies in the plasma may be present. Thus occasional abortions due to IBR may occur in immunized dams.^{12,16} Obviously more work and study is necessary to further clarify the pathogenesis of this disease.

The I.B.R.-I.P.V. virus tends to localize in lymphoid tissue.^{10a,25} Vulvar scrapings from cattle affected with the vulvovaginal form of I.B.R.-I.P.V. can be examined by means of the fluorescent antibody technique for the presence of virus. This virus could be demonstrated with the fluorescent antibody technique^{16,19,20} in the placenta of infected cows 3 days after the death of the fetus. This technique could also be used to diagnose the presence of virus in other infected tissues of the adult or fetal animal.

Control and treatment of I.B.R.-I.P.V., as with other infectious viral diseases, can be assisted by blood testing and isolation of new arrivals into the herd with a second sample taken one to two months later. Any animal with a positive titer should be considered as a potential carrier of the virus. In an outbreak, contact between animals should be kept at a minimum depending upon the facilities available on the farm. In cases involving the vulvovaginal or preputial form of the disease, breeding should be stopped for 3 to 4 weeks to prevent further spread. Local oily antibiotic preparations might be applied to the ulcerated mucous membranes of the genital tract in severe cases in dairy cows. In valuable cattle suffering from the respiratory form of the disease, antibiotics are often administered to prevent pneumonia or secondary bacterial respiratory complications. Supportive treatment and good nursing is imperative. In abortions due to I.B.R.-I.P.V. the fetus and its membranes should be destroyed and the cow isolated from other pregnant susceptible cattle for 3 to 4 weeks. If calves on a farm are infected and ill, pregnant cows should be kept from contact with them. If virus-free semen is desired, then I.B.R.-I.P.V. infection of donor bulls must be prevented.^{12,13,32} However because of widespread and latent I.B.R. infections, maintaining an artificial insemination stud free of IBR virus is impossible. Regular vaccination programs and frequent examinations of semen for the presence of IBR virus are now practiced.¹²

I.B.R.-I.P.V. modified live virus (MLV) vaccines are available either alone or in combination with B.V.D.-M.D. (Bovine virus diarrhea-mucosal disease) virus or

parainfluenza virus. Vaccines given intramuscularly may combine IBR and BVD viruses while those given intranasally often combine IBR and Parainfluenza (P13). Killed or inactivated IBR vaccines have been produced. These vaccines should be handled carefully and kept refrigerated so as to maintain their potency. Vaccine instructions should be read and followed carefully as certain vaccines should not be given to pregnant cows or to calves they are nursing. Severe signs of disease with diarrhea often was associated with natural concurrent I.B.R.-I.P.V. and B.V.D.-M.D. viral infections.^{10b,12} It is possible that severe clinical reactions in adult cattle following vaccination have occurred with the combined vaccines and where other diseases such as salmonellosis or B.V.D. are present and active at the time I.B.R.-I.P.V. vaccine is administered. These severe reactions may be associated with BVD virus which has an immunosuppressive potential in cattle. To provide protection against I.B.R.-I.P.V. virus, vaccination is best carried out in heifers at 6 to 8 months of age when a good immunity will develop that will last 3 or more years.¹² Vaccination if done earlier may be ineffectual because of maternal colostral antibodies often present in calves getting colostrum from immune dams. In recent years the M.L.V. vaccines, especially the intranasally administered ones that combine IBR and P13 viruses can be given to cows at any stage of gestation and even in the face of an outbreak. These are used routinely in an annual preventive vaccination and revaccination or "booster" program in many dairy and beef herds. Both intramuscularly and intranasally administered vaccines produce systemic antibodies within 7 to 14 days. The latter also produces a local antibody reaction and IgA which on challenge results in the rapid production of interferon titers.^{9,12,13}

Another bovine herpesvirus, Movar 33/63 type, was isolated along with BVD virus from an aborted 6 month old fetus.^{27b}

Bovine virus diarrhea-mucosal disease (B.V.D.-M.D.) virus was originally reported as a cause of abortion in over 20 percent of the cows from 2 to 9 months of gestation in 5 herds with severely affected cattle.^{11,19} Since 1946 few outbreaks have been recorded in N.Y. State and the clinical disease has been largely limited to a few young heifers, 6 to 24 months of age, in which the outcome is uniformly fatal.^{5,13,17} Serological surveys using serum neutralization tests to determine the incidence of antibody titers for the B.V.D.-M.D. agent in the cattle population have revealed an incidence of 50 to 70 percent B.V.D.-M.D. reactors in the U.S. and 20 to 50 percent in Europe.^{5,11,13,18} Thus cattle are the main reservoir of infection and most infections are inapparent as the clinical form of the disease is seldom observed.

Two herds experiencing an epizootic disease characterized by fever, depression, some anorexia and diarrhea in older lactating cattle were carefully studied. In one herd good circumstantial evidence indicated the disease was due to virus diarrhea and in the other herd serologic evidence confirmed the cause to be B.V.D.-M.D. virus. In the first herd 39 pregnancies terminated with 24 normal parturitions, 11 or 28% abortions, 2 early neonatal deaths and 2 live ataxic calves with cerebellar hypoplasia. In the second herd, 5 or 20% abortions occurred in 25 pregnant cows, 1 calf was "stillborn" and 2 calves had cerebellar hypoplasia. Abortions occurred 1 to 5 months or more after the initial epizootic and in the latter half of gestation. A few fetuses showed evidence of death, mummification and delayed expulsion from the uterus. Six months after the time of infection in the first herd, 97 percent of the animals had B.V.D.-M.D. antibody in their serums.^{9,10}

Dual I.B.R.-I.P.V. and B.V.D.-M.D. infections exhibit severe signs of disease.³ B.V.D.-M.D. virus from 2 aborted bovine fetuses 7 and 8 months of age was recovered.² The experimental evidence was cited that incriminated B.V.D.-M.D. virus as a probable cause of sporadic abortions. Eleven susceptible heifers at 5 to 7 months of gestation were infected with this virus recovered from an aborted fetus. One heifer calved prematurely, 3 calves had mild ulcerative mucosal lesions at birth referable to an intrauterine infection including one calf with cerebellar hypoplasia. Thus fetal lesions may resemble lesions seen in the mouth and digestive tract in older animals with the acute form of the disease.^{15,20} All calves in the above experiment had active B.V.D.-M.D. titers in their serum at birth and before colostrum ingestion. These titers persisted for over 6 months.

Kendrick^{12,13} has reported that BVD-MD virus is a mild virus for the fetus compared to the IBR virus. In all cows in which the fetuses were inoculated at 180 to 225 days of gestation, every fetus survived and showed no evidence of disease except the isolation of low levels of virus and the presence of a specific antibody to BVD in the fetal plasma. These antibodies were the result of an active immune response. When these calves were allowed to live, no virus could be recovered and the antibodies persisted for at least a year. When fetuses were inoculated with BVD virus at 150 to 170 days of gestation and examined a week later, they showed some evidence of disease, edema and hemorrhage, due to a vasculitis, moderate levels of virus but no antibodies indicating a lack of an immune response. Four weeks later the fetuses had recovered from the acute disease, virus was still present but no antibodies had developed. Later

in gestation the fetuses developed antibodies and the virus was eliminated. None of these fetuses had virus present at birth. When fetuses were inoculated with BVD-MD virus at 80 to 120 days and examined a week later, all were alive, some vasculitis was present and large amounts of virus was isolated. But between 7 and 14 days these fetuses died and most were aborted and a few became mummified. Viral infection of the fetus with BVD virus at 90 days of gestation causes necrosis of the dermis and partial alopecia if the fetus survives to term. Similarly fetuses infected at 125 to 150 days of gestation may develop necrosis of the external granular layer of the cerebellum producing cerebellar hypoplasia in the newborn calf. Also at this stage eye lesions and cataracts may develop.

In a recent study of the BVD-MD virus by Done and coworkers,¹ 15 pregnant heifers (1 with twins) with no antibodies for BVD-MD virus, were inoculated intramuscularly with combined field strains of cytopathic virus at 100 days of gestation. The heifers exhibited no clinical signs of disease but seroconverted within 6 weeks. Five heifers, including one with twins, had fetuses that died **in utero**. Four aborted about one week after fetal death 36 to 54 days after heifer inoculation. The other heifer had a mummified fetus. All aborted fetuses showed signs of growth retardation. The remaining 10 heifers produced live calves at term that were carefully cultured, examined serologically and autopsied. All 10 calves showed growth retardation and thymic hypoplasia. Four had C.N.S. malformations, 8 had spinal dysmyelination and 3 had microencephaly, internal hydrocephalus and/or cerebellar dysgenesis or hypoplasia. Two of the calves had specific serum antibodies against BVD-MD virus and no virus was recovered from them. But the other 8 calves had not seroconverted and a noncytopathic BVD-MD virus was recovered from these calves. These latter calves had developed either immunological tolerance or immunological paralysis. This study further indicates that the BVD-MD virus can be immunosuppressive. This study noted the great similarities between BVD-MD virus, Border Disease virus and hog cholera (swine fever) virus which are all pestiviruses. It further stressed the possible importance of the BVD-MD virus in the world, by indicating that potentially 1 in every 16 bovine fetuses in Britain was at risk from this virus. Because of the widespread presence of the BVD-MD virus and its immunosuppressive potential when associated with other bovine disease it may be one of the most important causes of economic loss to the cattle industry.^{4,16} Also related to this potential is the evidence that 0.5 to 1 percent of severe postvaccinal disease problems follow the administration of MLV, BVD-MD vaccines. BVD-MD

virus in newborn calves either contracted **in utero** or postnatally may cause enteritis and death.¹⁴

It is obvious, because of the widespread presence of this virus and serologic reactions in cattle, that a rise in titer or a titer going from negative to positive as determined by paired samples is necessary for a possible or probable diagnosis of BVD-MD abortion. Of 47 paired blood samples taken from cows at the time of abortion and two to three weeks later, 15 percent showed a rise in titer of BVD-MD antibodies.¹⁵ After a natural infection a lifelong immunity developed.^{5,6,11,12,13}

Commercial MLV vaccines are available that induce a permanent lifelong immunity when administered to calves at 6 to 10 months of age. Vaccination at an earlier age may be ineffective because of a passive immunity induced by the maternal colostral antibodies. Stressed cattle should not be vaccinated or the vaccine should be used with caution.^{5,6,11,13} Vaccination during pregnancy should be avoided. Dual IBR-IPV and BVD-MD attenuated vaccines tend to produce occasional or sporadic moderate to marked postvaccination reactions especially in stressed cows or calves.^{3,4,14} Some veterinarians recommend annual "booster" vaccinations after calving and 30 to 60 days before breeding.^{4,14} Inactivated BVD-MD vaccines have recently been marketed that may prevent the occasional reactions seen after using the MLV or attenuated vaccines. Further studies on BVD-MD vaccines and vaccination procedures are indicated.

Miscellaneous Viral Infections including Parainfluenza and Bluetongue associated with bovine abortions are usually sporadic unless highly susceptible cows at the proper stage of gestation are heavily exposed to a virulent virus. Most of the following viral diseases are inapparent or nonclinical infections in the adult animal.

Bovine myxovirus parainfluenza 3 (PI3) was recovered from an aborted bovine fetus and produced abortion in a pregnant cow 9 days after intrafetal inoculation.^{11,14} Signs of fetal septicemia with petechial hemorrhages were observed. Abortions have not been produced by virus inoculated by natural means. This virus is apparently widespread in cattle as serological studies have revealed it to be present in 50 to 95 percent of the cows.^{6,14} Viruses such as BVD-MD and bovine parainfluenza 3 are present so commonly in cattle that occasional isolations from fetuses might be accidental or in association with another agent that caused the abortion. Bovine parainfluenza 3 virus is usually associated with shipping fever pneumonia.¹¹ The virus alone is only a very mild pathogen and can be recovered from healthy cattle. Since most cattle are PI-3 seropositive and resist transplacental transmission of virus, PI-3 virus is not a common cause of fetal disease and abortion. **In utero**

inoculations of bovine fetuses with PI-3 virus cause fetal disease and fetal immune competency.¹⁴ PI-3 virus may be a more important cause of abortion in dairy herds in northeastern United States because PI-3 antibody was demonstrated in 53 percent of aborted fetuses and 29 percent had PI-3 antibodies in combination with other antibodies.³ MLV vaccines for immunizing calves and cows against parainfluenza-3 alone or in combination with other viruses, such as IBR, are commercially available for intramuscular or intranasal use.^{11,6}

Bovine enteroviruses—In 100 aborted bovine fetuses, 5 to 8 months of age, examined only 27 definitive diagnoses of the causative agent could be made. However, serologic studies on these 100 fetuses revealed antibodies to PI-3 in 53 percent and enterovirus in 41 percent often combined with antibodies against other viruses.^{3,4} Enteroviruses and parvoviruses can cause fetal deaths in swine. Further studies on the role of enteroviruses in bovine abortion is indicated. Evidence for this agent as a cause for abortion has been reported from England and the United States.^{3,4}

Bovine parvovirus is common in some areas of the United States with 65 percent of cows carrying antibodies.^{1a,b,12} Fetal inoculation with parvovirus during the first trimester of gestation resulted in growth of virus in the fetus and abortion. Fetuses inoculated during the second trimester became infected with the virus. Fetuses inoculated during the third trimester developed antibody titers and no virus was recovered. A cow pregnant about 175 days was inoculated with bovine parvovirus and aborted a partially mummified fetus about 80 days later and virus was identified in the fetus and resulted in a latent uterine infection.^{1b,12} Further study on the lethal effects of bovine parvovirus on fetuses is indicated.

Bluetongue virus of sheep, goats and cattle which is widespread in tropical and semi-tropical climates and in the western and southern half of the United States has been reported as a cause of abortion^{4,11,1a,9,10a} as well as congenital defects described in Chapter III. The disease is spread naturally by insect vectors, particularly gnats, *Culicoides variipennis*. This insect vector is responsible for the geographic distribution and seasonal occurrence of the disease. Elk, white-tailed deer and other wild ruminants are susceptible to bluetongue virus and may be long-term carriers or potential reservoirs of the virus.^{6b} Bluetongue is not a problem in cold climates because the *Culicoides* vectors that spread the disease cannot survive. New Zealand and Australia are presently considered free of the disease. Most cases of bluetongue in cattle, which are considered to be the reservoir host, are subclinical but occasionally severe cases exhibit a characteristic elevated temperature, drop in milk production,

ulcers in the mouth with slobbering, ulcers on the teats and inflammation on the muzzle and coronary band with lameness. There are four serotypes of bluetongue virus in the United States,^{4,7,9,10} and 20 in other world countries.^{10b} Following infection a viremia occurs lasting several weeks during which the virus may pass to the embryo or to the fetus, especially in early or midgestation, and cause its death with abortion or mummification or cause fetal disease especially of the central nervous system with hydranencephaly, contracted, deformed extremities, or the birth of apparently normal immunological tolerant calves that are latent carriers of the virus.^{4,7,8,9,10} Bluetongue virus may be found in the semen of apparently normal bulls and be transmitted to the cow at the time of breeding.

Fourteen susceptible heifers were bred naturally to a bull shedding bluetongue virus in his semen.⁸ All heifers developed viremia but no clinical signs were observed. Twelve heifers conceived on the first service but one aborted about 60 days of gestation. Two heifers were rebred twice at irregular intervals before conceiving. Only one of the 14 heifers developed a precipitating antibody to bluetongue virus. Thirteen of the 14 heifers calved with gestation periods of 281 to 297 days. All twelve calves born were viremic and had congenital anomalies and five of these were weak and ataxic at birth. Thus natural service, and probably artificial insemination of semen infected with bluetongue virus by a carrier bull is an effective nonvector-mediated means for the spread of bluetongue virus in cattle.⁸

The complement fixation test, SN, ELISA^{10b} and agar gel immunodiffusion (AGID) tests are used to detect antibodies indicative of prior infection. Virus isolation and immunofluorescent procedures can also be used for virus identification in cows and fetuses. In the United States there is only one M.L.V. vaccine containing only one serotype approved for use against bluetongue in sheep but none for cattle. Work is in progress on an inactivated or killed bluetongue vaccine for sheep and cattle.¹³

Pseudorabies or Aujeszky's disease or malignant catarrhal fever caused by a herpesvirus may result in abortion if the pregnant affected cattle do not die within a few days of the onset of the disease. A new herpesvirus and a cytomegalovirus were reported to have been recovered from aborted bovine fetuses.^{2b} Since more recent reports on these agents have not appeared, the earlier, apparently rare findings, are of limited importance. Prenatal transmission of **bovine leukemia virus** is uncommon and abortions due to this virus have not been reported.^{4b}

Foreign bovine diseases, not presently in the United States but associated with abortion, include **foot and**

mouth disease, rinderpest, Rift Valley fever,^{4,11,16,24} and Akabane virus disease.⁵ This latter disease in its mode of spread and its effects on the late embryo and fetus closely resembles bluetongue virus disease. Abortion, stillbirths, premature births, hydranencephaly, and arthrogryposis occur depending on the stage of gestation when infection of the fetus occurred (See Chapter III). Akabane disease has been reported in Japan, Australia and Israel.

Mycotic or Fungal Causes of Abortion

Almost all mycotic bovine abortions or internal mycoses are caused principally by two groups of fungi. About 60 to 80 percent are caused by *Aspergillus* spp. and most of these are *Aspergillus fumigatus*.^{3a} The *Mucorales* order of fungi, especially *Mucor pusillus*, are responsible for most of the remainder of mycotic abortions. Other uncommon fungi include: *Allescheria boydii*, *Torulopsis glabrata*, *Mortierella wolfii*, *Absida ramosa*,^{3a} *Cephalosporium*¹⁰ and rarely the yeast *Candida tropicalis*.^{11,12,13} The incidence of bovine mycotic abortion varies from 4 to 20 percent of all diagnosed infectious bovine abortions.^{13b,18,12} The higher incidence is noted in areas where brucellosis and vibriosis have been controlled. Most mycotic abortions are sporadic but the author has observed a number of small herds having 3 to 5 mold abortions, up to 5 to 10 percent of the herd, in a winter season.

Aspergillus, *mucor* and other molds are ubiquitous in nature and are usually saprophytic. Occasionally they may localize in the body producing serious systemic diseases. The highest incidence of mycotic abortion occurs in the winter months^{13b,4,6,12} often following a wet summer season when the hay and straw was baled while damp and mold developed. One study found no correlation between total rainfall or rain days during the months that hay was baled and the incidence of the disease the next year. However, the abortion rate was highest in cows fed in cowsheds.¹² Molds apparently are taken into the body by inhalation into the lungs or by ingestion. The mold spores are then carried to the placenta in the bloodstream from lesions in the respiratory tract or ulcers, mycotic rumenitis or other lesions of the digestive tract. This results in a slowly developing fungal placentitis, interference with the nutrition of the fetus, fetal death and abortion after a number of weeks or months. Abortion occurred about 35 days after the intravenous inoculation of spores of *Aspergillus fumigatus*.⁴ Most mycotic abortions occur about the 5th through the 8th month of gestation but may occur from the second month to

term.^{3b,4,6,12} A few live normal calves have been born with a placenta having a severe mycotic placentitis. The fetuses in most mycotic abortions show evidence of growth retardation. The fetus is usually expelled dead with a degree of autolysis present but in some cases premature or full term calves are alive but weak at birth and die shortly thereafter. Mycotic infections could not be established by the intrauterine infusion of *Aspergillus fumigatus* spores at the time of insemination. The non-gravid uterus appeared quite resistant to mycotic infection.⁵

Mycotic abortion is usually characterized by marked gross changes in the fetal membranes resembling, but much more pronounced than, those due to **Br. abortus**, **C. fetus** and chlamydia.^{15,7,8} The chorion is thick, edematous, leathery, and necrotic. The primary lesions are in the placentomes. Both the maternal caruncle and fetal cotyledon are very large, swollen, edematous, and necrotic. The enlarged cotyledons may be firmly incarcerated and resist detachment for 8 to 10 days or more after abortion. The placentomes may then become completely detached due to severe necrosis involving the cotyledons, caruncles, and the caruncular stalks. In a few instances these necrotic structures remain in the uterus for several months after abortion or normal birth and retained placenta, and resemble a macerating fetus and/or pyometra. The cow must often be sold as sterile.

The necrotic cotyledons show a dull grey center surrounded by areas of hemorrhage and are firmly attached to the leathery chorion. In the uterochorionic space is usually some reddish fluid with large flakes of pus. The fungus spreads by extension through the fetal membranes to the fetal fluids. The fetus may be normal in appearance or in about 30 percent of the cases, mold may grow on the skin in patches or plaques that resemble congenital ichthyosis or ringworm.^{4,12} (See Figure 63.) Straw-colored serous fluid may be present in the fetal tissues or body cavities. In rare instances the liver is enlarged and swollen. The mold can often be recovered from the stomach contents or from the diseased chorion or cotyledons of the placenta. In a few fetuses the lungs are involved with a mycotic bronchopneumonia and the brain with a mycotic granuloma.^{3b} The endometrium is as severely involved as is the chorion but even with this severe uterine infection, generalized symptoms of septic metritis are seldom exhibited. Recovery in severe cases may be slow and prolonged or permanent sterility may follow. In one study 80 percent of the cows conceived after mycotic abortion but conception rate on first service was only 33 percent.¹²

The diagnosis is confirmed by histologic examination of the placental or fetal tissues and by culture of the mold on artificial media. In submitting specimens to the lab-

oratory for diagnosis it is imperative to include placental tissues as frequently the placenta is severely affected by mold but the fetus is not infected.^{9,12,13}

Infectious Parasitic Protozoal Causes for Bovine Abortion

Trichomoniasis due to *Trichomonas fetus* is a venereal disease characterized, as is campylobacteriosis (vibriosis), by infertility and early embryonic death. Abortions due to trichomoniasis usually occur during the first trimester or through the fourth month of pregnancy. Abortions after the fifth month of pregnancy are rare. For this reason retained placenta is uncommon in trichomonad abortion. Observed trichomonad abortions are uncommon. The disease is fully discussed in Chapter XII on Infertility in Cattle.

Abortions in cattle due to other parasitic protozoa are uncommon. These protozoa, except the anaplasma, are members of the order of Coccidia. The sporocysts are passed from the intestine of carnivores, especially cats and dogs, and when ingested by other animals invade the body tissues producing disease.^{4,2,5b,9,11} These parasitic protozoa include: *Toxoplasma gondii*, *Sarcocystis* spp. and *Besnoitia besnoiti*. The latter organism is apparently limited in occurrence to southwest Europe and Africa while the other two organisms have a worldwide distribution. Cattle, in contrast to sheep, are rather resistant to toxoplasmosis and abortion due to *Toxoplasma gondii* is rare if it does occur naturally.^{4,1,11,12}

Anaplasma marginale has been described as a cause for abortions in cattle when susceptible cattle are acutely infected the third trimester of pregnancy.^{8,14,16} Transplacental transmission of anaplasma to the fetus is uncommon. In further trials susceptible pregnant heifers inoculated with *A. marginale* the second trimester of pregnancy did not abort.^{15,16} Thus it is likely that abortion late in gestation due to acute *A. marginale* infection occurs secondarily to the acute anemia of the dam with fetal acidosis, anoxia, and death, when fetal demands for oxygen are elevated as compared to the oxygen requirements of fetuses during for second trimester of pregnancy.¹⁴ This hypothesis is further supported by evidence that severe anemia secondary to a heavy sucking louse (*Haematopinus eurysternus*) infestation also causes bovine abortion in late pregnancy.¹⁴ A further experiment repeating these studies and including hormonal studies, especially of fetal and maternal cortisol levels would be most interesting and informative. Four injections IM of a long-acting oxytetracycline (20 mg/kg) at

3-day intervals eliminated the naturally-infected anaplasmosis carrier state in 14 cattle.^{11c} Further studies are indicated.

Abortions due to *Sarcocystis cruzi*, *bovicanis* and others and *Toxoplasma gondii* have been produced experimentally in cattle by massive exposure to sporocysts and tachyzoites of these respective protozoa.^{5b,c,d,7a,b,11a,b,c,12,13} In abortions following experimental exposure to *Sarcocystis* no organisms were found in the dead fetuses but migratory merozoites were found in the uterine caruncles.^{6,9} Abortions have been described in the last trimester of pregnancy in severely affected naturally-occurring outbreaks of sarcocystosis (Dalmeny disease or rat-tail syndrome).^{7a,b,9,11a} The severity and chronicity of this clinical disease leads one to suspect hormonal changes due to stress to be a possible cause of abortion. However recent reports have described sarcocystis organisms throughout the aborted fetus, especially in the endothelium and brain.^{7a,11a} Abortions did not occur in pregnant cattle fed toxoplasma oocysts from cat feces. It was concluded that abortions in cattle due to toxoplasmosis were unlikely, but infected weak, stunted calves with congenital chorioretinitis might occur.^{1,12}

Besnoitia besnoiti causes a severe extensive dermatitis, diarrhea, debility and a low mortality rate.^{4,2} Abortions in pregnant cows and sterility in bulls is reported in bovine besnoitiosis.^{4,2} *Trypanosoma theileri* has been recovered from the stomach of an aborted bovine fetus.⁶ **Babesiosis** or piroplasmosis due to *Babesia bigemina* and *argentina* may cause abortion if an adult pregnant female cow is severely affected by fever, hemoglobinemia, jaundice, anemia and loss of condition.⁴



Figure 63. *Aspergillus fumigatus* or mold infection of the skin of an aborted 7-month bovine fetus.

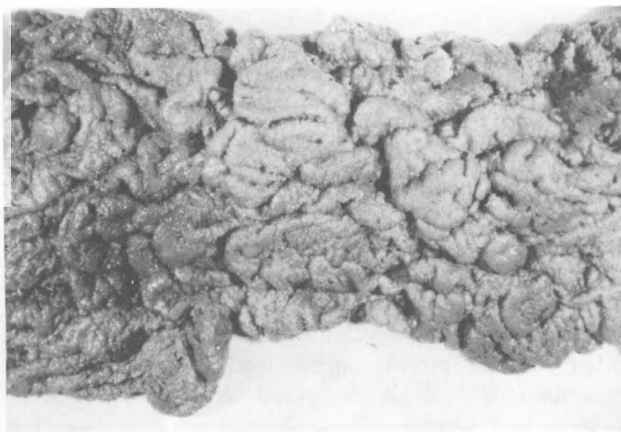


Figure 64. *Aspergillus fumigatus* or mold infection of the equine fetal placenta (courtesy K. McEntee).



Figure 66. Torsion of the umbilical cord of a 6-month bovine fetal cadaver undergoing early mummification.

Abortions in Animals Infectious to Humans

With more women entering the field of veterinary medicine, attention should be called to the infectious diseases capable of causing abortion in both animals and man: brucellosis, listeriosis, campylobacteriosis (vibriosis), mycoplasmosis, ureaplasmosis, chlamydiosis, toxoplasmosis, possibly leptospirosis and salmonellosis and others.^{3,5a,5c} All of these infectious causes of abortion or teratogenicity have been reported in most of the species of large and small domestic animals. Veterinarians are frequently called upon to care for aborting animals and treat the secondary retained placenta and metritis that often follows the abortion without a knowledge of the causative agent. It behooves all veterinarians, especially pregnant ones, to take careful hygienic and other precautions

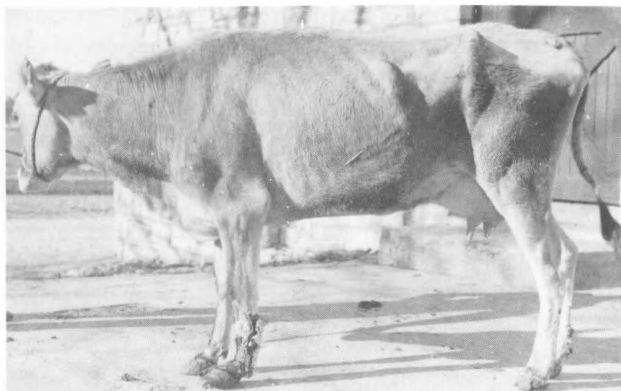


Figure 65. Chronic ergot poisoning of a Jersey cow carrying a normal 6-month fetus.

to avoid exposure to these agents infectious to man and human fetuses.

Chemicals, Drugs and Poisonous Plants as Causes for Abortions in Cattle

Nitrate poisoning ("lowland or marshland abortion") was originally described in Wisconsin as occurring in cattle pastured on unimproved weedy muckland pasture.^{27,28} Up to 80 percent abortions in a herd occurred from 3 to 9 months of gestation and no infectious agent was found. When these pastures were improved by treating with herbicides and fertilizer to promote the growth of grasses abortions no longer occurred. It was considered that nitrate concentrated in certain plants was possibly the cause of abortions. Workers in Missouri^{17,30} published extensively on the progressive stages of nitrate intoxication including the lowering of the vitamin A levels, loss of production and abortion. In the early 1960's extensive experimental studies and reports^{3,4,5,17,32} demonstrated that low to fairly high levels of nitrates in the feed produced no harmful effects on cattle or caused abortions. A few abortions in experimental cattle and in field outbreaks were produced but they were associated with very high levels of nitrate ingestion producing severe toxic reactions, marked methemoglobinemia and occasional death.^{2,4,29} Since experimental nitrate feeding produced levels of 65 to 75 percent methemoglobin without respiratory distress in pregnant heifers^{4,29} and fetal oxygen tensions are normally only 20 to 30 percent of adult values, fetal hypoxia might have been the cause of fetal death in heifers given near lethal doses of nitrate.

Chlorinated naphthalenes formerly used in lubricants produced hyperkeratosis or X disease and an acute vitamin A deficiency characterized by dry, thick, wrinkled skin, metaplasia of the epithelium of many internal structures and glands, metritis, abortion, dystocia and retained placenta.¹¹ The occurrence of this disease in recent years has been rare.

Chronic arsenic poisoning has been reported to be a cause of abortion.³¹ Although **lead** poisoning has been associated with abortions in humans it has not been reported in animals.

Sodium iodide given in large doses intravenously has occasionally been reported as causing abortion in pregnant cows.^{9b} Sodium iodide injected in large doses often causes a rise in body temperature, depression, and anorexia. The author has on numerous occasions administered sodium iodide to pregnant cows without abortion resulting. Another study also reported that sodium iodide given intravenously failed to cause abortion in cows.²¹ However a recent report indicated an organic iodide, ethylenediamine dihydroiodide, when fed dairy cows at approximately 1000 times the daily requirement for 30 days resulted in 12 abortions, or 20 percent of the herd, within 68 days. Abortions occurred in 66 percent of the cows from 1 to 90 days of gestation but in only 9 percent of the cows over 180 days of gestation. No infectious causes of abortion were detected.²³

Locoweeds (*Astragalus lentiginosus* and *Oxytropis sericea*) caused abortions in cattle when ingested at any stage of the gestation period. The rate of abortions was related to the amounts of the plant ingested and the severity of the poisoning.^{13,14,15,18} No typical lesions were observed in the aborted fetus or membranes but some evidence indicated the fetuses suffered from malnutrition possibly related to placental changes. Consuming lesser amounts of locoweed resulted in deformed fetuses with rotation and ankyloses of the limbs. Sheep were similarly affected. This plant was habituating and animals would eat it even when good grass was available. In advanced cases neuronal degeneration and emaciation developed, due to the indolizidine alkaloids.^{24b} Many nitro-containing and selenium accumulating varieties of *Astragalus* are not abortifacient.¹³

Perennial Broomweed (*Gutierrezia microcephala*) when ingested caused 10 to 60 percent of the fetuses in affected herds to be expelled prematurely either dead or weak at birth. Calves were small, 8 to 50 lbs., and retained placentas were common. A variation in the toxicity of the plant grown in different types of soil was noted. Abortions were due to a saponin in the plant.^{6,7}

Sweet Clover Hay or Silage may cause fatal fetal hemorrhage due to the action of dicoumarol. None of 14

calves born to dams fed sweet clover hay survived for more than a few hours. The cows were not affected. Elimination of sweet clover hay from the ration resulted in a cessation of losses. The toxic compound is produced by fungi growing in moldy sweet clover hay. Neither this nor any other known mycotoxin is actually abortifacient.¹⁹

Pine needle (*Pinus ponderosa*) ingestion causes abortion in cattle from 21 to 142 days after the ingestion of the pine needles in the Western United States and Canada. A recent report indicated abortion may occur after only one or two days of feeding pine needles especially if the cow was stressed.¹² Abortions may occur from 6 to 9 months of gestation. Many affected calves are born prematurely, small and weak and die soon after birth. Retained placentas and metritis are common. The toxic agents which are heat labile are probably diterpene resin acids.^{20a} Vitamin A levels in aborting cattle are normal.^{1,9a,12} Pine needle abortion resembles closely perennial broomweed abortion.¹²

Ergot poisoning due to the consumption of *Claviceps purpurea*, a fungus that grows on rye, wheat, barley and many grasses, has been reported to cause outbreaks of bovine abortion. These reports in most cases were in error as abortion is not a feature of ergot poisoning in cattle.^{19,34} In cattle and humans large continued doses of ergot result in gangrene of the extremities and central nervous disturbances.^{10,19,25,34} The author has observed, as did the latter authors, cows with gangrene of the extremities still maintaining a normal pregnancy. (See Figure 65.) There are 6 or more toxic principles, mostly alkaloids, produced by ergot. Ergonovine, which is one of these produces an oxytocic effect on uterine muscle that lasts a number of hours following a single dose. Tall fescue grass, *Festuca arundinacea*, infected with a fungus containing alkaloids similar to ergot,^{2b,16,18,19} which when consumed by cattle caused a similar necrosis of the extremities. No abortions have been reported in these cattle. Recent studies indicate that a mycotoxin produced by an endophytic fungus in fescue hay or seed, not a plant alkaloid, is the agent causing fescue toxicity.^{26b} Ergotism was produced in pregnant sows by feeding barley containing 1 percent ergot. No abortions occurred in the sows but the pigs were weak and small and the sows had a lack of udder development and agalactia. Agalactia has been reported in other species of animals that have consumed ergot.^{20b,24}

Polybrominated biphenyls (PBBs) when fed at high levels to pregnant heifers and cows caused toxic clinical signs, resembling chlorinated naphthalenes or X-disease, including anorexia, lacrimation, salivation, diarrhea, emaciation, dehydration, depression and abortion with

an autolyzed fetus and a necrotic placenta. Metritis and retained placentas were common in cattle aborting from 5 months to term. All animals became moribund within 33 to 66 days.^{8,22}

Pesticides including **Diazinon**, **Sevin**, **Marlate**, **Ciodrin**, **Vapona**, dieldrin, DDT, **Epoxide** and other organic phosphates were studied and no evidence was found that they contributed to the incidence of abortion on Wisconsin dairy farms.³³

Although **dietary urea** has been suspected of having a possible effect on bovine reproduction including abortion, no studies have shown a definite effect when urea is fed at recommended levels.

Hormonal Causes of Abortion in Cattle

Estrogenic compounds if given in large doses over a period of time will cause abortion in cattle by causing regression of the corpus luteum.^{9,21} The injection of 100 mg of **Repositol** diethylstilbestrol intramuscularly to pregnant heifers up to 4 months of gestation and 25 mg more for each additional month of gestation produced abortions in 3 to 12 days after the injection in 79 percent of 761 heifers. Those that failed to abort were retreated with slightly larger doses and 50 percent of those aborted after the second treatment.⁹ Retained placentas and metritis occurred in some cows aborted in late gestation. For this reason inducing abortion between 5 to 9 months, especially with large or repeated doses of estrogens, should be undertaken with caution.⁴ Abortions were produced in 19 heifers pregnant 2 to 6 months with 80 mg. of stilbestrol in oil given twice at 3 day intervals.³ Similar results can be expected with high doses, or repeated doses, of estradiol cyclopentylate (E.C.P. or cypionate), aqueous suspensions of estrogens, pellet implants of estrogen or even high levels of orally ingested estrogens. Abortions occurred in heifers fed silage sealed with manure from hexestrol-fed steers.¹⁶ Abortions in 13 of 33 cattle from 105 to 204 days of gestation were reported after consuming poultry litter from birds being fed grain containing dienestrol.⁸ Much estrous activity was exhibited by the herd during this same period. When feeding of the poultry litter stopped, abortions and the estrous activity ceased. Estradiol valerate, at a dose level of 20 mg intramuscularly, at 60 to 120 days of gestation caused abortions in 8 of 10 heifers between 8 and 16 days after injection. A second injection of estradiol caused abortion in the two heifers not aborting after the first injection.⁶ Single moderate doses of estrogen such as 20 to 40 mg. of stilbestrol or 2 to 4 mg of estradiol have not produced abortions on experimental injection into pregnant cattle.

If large doses are administered to cattle to overcome anestrus, the uterus should be carefully palpated per rectum to make certain that pregnancy is not present. Abortion under these circumstances can be highly embarrassing for a veterinarian even though the owner did not know the animal was pregnant and reported her to be anestrus.

The **glucocorticoids** or **hydrocortisone** may cause abortion in cattle. The close relationship between the adrenal cortex and the maintenance of pregnancy has been reviewed.¹⁸ The gonads and adrenals have a common embryological origin and produce steroids that are chemically similar and closely related. The adrenal gland can readily convert progesterone and androgens into cortisone and cortisol. Prolonged gestation in Holsteins and Guernseys, as discussed previously, are caused by inherited fetal defects including hypoplastic adrenal glands and adeno-hypophyseal hypoplasia or aplasia resulting in a failure to produce cortisone essential for normal parturition (See Chapter VI). Parturition was induced in 9 cows with prolonged gestation, 290 to 349 days, with one or two injections of 10 to 20 mg. dexamethasone and 10 to 50 mg. estriol. Abnormal calves with aplastic adrenal and pituitary glands were expelled one to three days later.^{9c}

Five heifers, pregnant 193 to 222 days, were given recommended amounts of glucocorticoids for 4 to 8 days; 4 heifers were injected with 5 mg daily of flumethasone and 1 heifer received 2 boluses orally daily of dexamethasone, 5 mg per bolus. All heifers aborted between the 4th and 13th day after the start of the experiment; one fetus was undergoing beginning maceration.¹² The injection of 20 mg of dexamethasone intramuscularly into 22 cows, 235 to 280 days pregnant, resulted in 19 calving or aborting within 22 to 56 hours or an average of 45 hours.^{1,2} Three of 5 cows under 260 days of gestation failed to calve or abort. All but one of the cows produced live calves but only 2 of the 22 treated animals dropped their afterbirths normally. Within 24 hours after the injection the vulva was swollen and relaxed and the udder had filled with milk. In a subsequent study it was concluded that dexamethasone most successfully induced parturition from day 255 of gestation to term. Induction failure increases as the length of gestation decreases.^{1,2} Estrogens and especially glucocorticoids might well be indicated to produce abortion in occasional cows with a prolonged gestation. It is interesting to speculate on the role of stress and increased cortisone production on abortions or premature births in cows in late gestation that occur following severe systemic diseases, malnutrition or starvation, severe prolonged physical work or long distance transportation to shows or fairs. Administration

of cortisone the last few weeks of gestation should be avoided unless premature births are required.

Prostaglandins either prostaglandin F_{2a} ("Lutalyse") or prostaglandin analogues cloprostenol ("Estrumate") and others are excellent compounds used in cycling cows to induce luteolysis or involution of the corpus luteum for estrus synchronization and in pregnant cows to induce abortion or evacuate the uterus in cases of mummified fetuses or pyometra. A prostaglandin analogue, 250 and 500 μ g. of cloprostenol, injected into pregnant heifers was a safe and effective abortifacient up to day 120 and from day 121 to 150, respectively. Most heifers aborted 3 to 4 days after the injection.^{21,22} Fifteen heifers 29 to 52 days pregnant aborted before 72 hours after the administration of 15 or 30 mg of PGF_{2a} .¹³ Two daily doses of 12.5 and 25 mg PGF_{2a} injected into heifers at 60 to 120 days of gestation caused 10 of 10 heifers to abort an average of 3.6 days later.⁶ A dose of 27 mg PGF_{2a} would be expected to produce an abortion rate of 85 percent in pregnant heifers less than 150 days into the gestation period.¹¹ Since inducing abortion in heifers over 150 days pregnant was inconsistent and unsatisfactory, even when larger doses of prostaglandin were administered, a combination of cloprostenol (500 mg) and dexamethasone (25 mg) was given to Group I, 37 heifers, 1 to 4 months into gestation, Group II, 40 heifers, 4 to 6 months into gestation, Group III, 40 heifers, 6 to 8 months into gestation. Group IV, 30 heifers, 1 to 8 months into gestation were not given any injection. In Group I all heifers aborted; in Group II and III 37 of 40 heifers aborted with 2 heifers diagnosed with mummified fetuses and one pregnant in each of these two groups. No abortions occurred in Group IV.⁵ Mummification instead of abortion may have been due to incomplete regression of the corpus luteum. Thus prostaglandins alone in adequate dosage regularly terminate pregnancy in cattle the first five months of gestation and the last month of gestation. During 5 to 9 months of pregnancy, high doses of prostaglandins should be combined with high doses of cortisone to induce abortions or terminate pregnancies. Apparently prostaglandin acts to greatly reduce the ovarian source and dexamethasone the uterine source of progesterone to bring about abortion.^{9b} If single products are used repeatedly large doses may be necessary until desired results are obtained. Greater complications from dystocia, retained placentas and metritis should be expected when abortions are induced between 6 and 8-1/2 months of gestation. (See Induction of Parturition.)

Progesterone deficiency appears to be a cause of early abortion in cattle but confirmed cases have not been described. Enucleation of the corpus luteum will regularly cause abortion when performed the first 160 days of ges-

tation.^{4,21} Maintaining pregnancy by the supplementation of existing progesterone levels during pregnancy by the parenteral injection of 500 mg of **Repositol** progesterone every 7 to 10 days starting 20 to 30 days before the expected abortion until 180 to 230 days of gestation in habitually aborting cows provides circumstantial evidence that a lack of progesterone may be the cause of the abortion. Improved embryo survival rates were also observed in ovariectomized gilts maintained on higher daily doses of progesterone, 80 to 160 mg. vs. 40 mg.⁷ About 1000 mg of **Repositol** progesterone every 10 days was required to maintain pregnancy from 30 to about 100 days of gestation and 500 mg after 100 days when the corpora lutea were removed from cattle.^{14,20} Abortions due to progesterone deficiency occurred at 45 to 180 days, but most often, 83 percent, prior to 100 days of gestation. The same cow tended to have repeated early abortions. At these times a large follicle may develop possibly resulting in a high estrogen level and involution of the corpus luteum and abortion. These cows appear to have an unstable endocrine constitution. Possibly improved techniques now available will permit more careful monitoring of the progesterone level in the serum during pregnancy in these animals and thus aid in determining whether an actual progesterone deficiency does occur in cattle. Reduced levels of plasma progesterone were noted after fetal death and prior to abortion caused by experimental inoculation of **C. fetus** into pregnant cows the last half of gestation.¹⁵

Oxytocin given during gestation will not cause abortion in animals. In humans and mares the latter hormone has been used by the slow intravenous drip method to induce labor once certain preparturition changes have occurred including the suitable relaxation of the cervix. This technique shows promise in horses for inducing parturition after the genital tract is relaxed and the udder contains colostrum (See Chapter VI). Oxytocin given daily to a cow on days 2 through 6 after service will interfere with luteinization resulting in a short estrous cycle of 8 to 12 days. Such a treatment would probably prevent conception.²¹

Nutritional Deficiencies as a Cause of Abortions in Cattle

Nutritional deficiencies may occasionally be a cause for abortion. The response of both wild and domestic animals to their food supply is markedly reflected in their reproductive processes. If food supply is low, reproduction either is greatly reduced or ceases under these adverse conditions. Prolonged malnutrition results in a ces-

sation of the estrous cycle and failure of conception. Acute severe starvation may result in abortion in pregnant cattle. It is very difficult to assess the more specific effects of nutrition on reproduction because only a few nutrients exert a direct effect on reproduction.³ In many cases animals are suffering from multiple deficiencies and thus present a confusing picture. Much of the data is not based on carefully controlled experiments, or is based on too limited a number of animals.

Multiple deficiencies brought on by starvation during the severe drought in the Midwest in the 1930's caused many cattle to become extremely emaciated and cachectic, resulting in a high incidence of abortion and birth of dead, weak, or premature calves. Animals on a very low plane of nutrition abort as a protective mechanism to conserve their own body reserves. Hyperplasia of the adrenals and elevated cortisol levels may be present.

Vitamin A deficiency adversely affects reproduction in all species. Pregnancy usually terminates in abortion late in pregnancy, or in the birth of weak or dead young.⁴ As mentioned previously severe vitamin A deficiency may cause birth defects especially involving the eyes. The female animal requires more vitamin A than does the male, and the pregnant female apparently requires more vitamin A than does the nonpregnant female.³ Vitamin A deficiency causes keratinization of the vaginal epithelium and degeneration of the placenta leading to abortion. If pregnancy goes to term, birth may be difficult and infection and retained placenta follow. Under range conditions protein, phosphorus, and carbohydrates, as well as vitamin A, are likely to be deficient.

An iodine deficiency and the associated hypothyroidism in cattle has been reported to cause weak or dead calves at term and abortion in cattle.¹ **A possible selenium deficiency** was described in northeastern California characterized by the birth of dead, weak or premature calves, as has been described in sheep, and a high incidence of retained placenta that appeared to respond to the injection of a therapeutic dose of selenium.^{2b} In a group of 18 yearling Chianina heifers with myodegeneration due to a combined vitamin E and selenium deficiency in Pennsylvania, 2 aborted, 8 calves were still-born or died within 48 hours and 7 of the heifers with periparurient recumbancy died or were euthanized.^{2a} There is no evidence that other vitamin, mineral, protein or other nutritional deficiencies will cause abortion in cattle.

Physical Causes for Abortion in Cattle

Douching the uterus by invading the cervix and rupturing the fetal membranes,⁵ with a pipette or catheter

and introducing 50 to 100 ml. of a weak, Lugols' solution (1 to 2 ml per 100 ml of water), 200 ppm chlorine solution or a mild potassium permanganate solution or other aqueous or oily antiseptic solutions from 7 to 60 days of gestation will usually induce abortion in the cow without producing a severe metritis. If this practice is followed the third or succeeding months of gestation complications may arise including metritis or fetal maceration. Intrauterine insemination or douching should never be performed if the cow is pregnant as this act often results in abortion. All cows inseminated for the second or subsequent times should have the semen deposited in the mid-cervical region.

Manual rupture of the amniotic vesicle or rupture of the fetal heart or large vessels by manual pressure on the amniotic vesicle in early pregnancy, 30 to 60 days of pregnancy and division of the fetus after rupture of the amniotic vesicle at 60 to 70 days will terminate pregnancy.^{2,5} In some cases the fetal membranes persisted and even grew for 2 to 3 weeks before resorption or expulsion. The latter was rarely observed. Thus estrus may not occur for a month or longer after the death of the embryo. The dangers of abortion by failure to handle the amniotic vesicle gently when it is easily traumatized during pregnancy diagnosis at 35 to 45 days of gestation, requires emphasis. Palpation of the amniotic vesicle as a diagnostic aid in early pregnancy examinations should be avoided by all but skilled examiners. After 45 to 50 days of gestation it is much more difficult to damage the amniotic vesicle by routine pregnancy examinations. To prevent twinning rupturing the amniotic vesicle of one of the embryos at 33 to 45 days of gestation has been attempted.^{4,5} In two experiments about 50 to 70 percent of the pregnancies terminated with estrus recurring in 4 to 8 weeks even though only one amniotic vesicle was crushed.

Three manual methods of inducing abortion early in gestation that can be applied to the conceptus per rectum are: rupture of the amnion and crushing of the embryo or fetus from 35 to 66 days of gestation, decapitation of the fetus in cows 66 to 120 days into gestation and rupture of the amnion without crushing the fetus in cows less than 70 days of gestation.^{1,3} All cows aborted between 10 and 54 days, with a mean interval of 21 to 27 days, after treatment except 3 of 29 cows in which only the amnion was ruptured. Mummification of the fetus occasionally occurred following fetal decapitation. It was difficult to rupture the amnion after 65 days and to decapitate after 90 days of gestation.

Removal of the corpus luteum of pregnancy in the cow invariably results in abortion. Removal of the corpus luteum to bring a cow into estrus should never be

performed without a careful examination of the entire uterus to detect a possible pregnancy. Probably waiting until the fourth week after service to be sure the cow has conceived is indicated before the corpus luteum is removed by manual manipulation of the ovary through the rectal wall when abortion is desired.⁵ This technique should be employed before the fifth or sixth month of pregnancy since by this time removal is difficult or impossible because the ovary is pulled forward and downward out of reach. After the sixth month, abortion may not occur and dystocia may result, particularly in heifers. It is advisable to watch the cow for symptoms of estrus and abortion after removal of the corpus luteum, to make sure that abortion has occurred. In exceptional instances abortion may not result because all of the corpus luteum might not have been removed, or another corpus luteum may be present in the opposite ovary.

Other miscellaneous physical causes for fetal death and abortion in cattle include **severe torsion of the uterus**, more than 180° and **rare displacements of the umbilical cord** over the head and neck of the fetus or **torsion of the umbilical cord** causing fetal death by interference with the circulation of fetal blood. (See Figure 66.)

Occasionally abortions in cattle are observed following severe transportation fatigue, severe systemic diseases and major operations such as for traumatic gastritis late in gestation. Excess production of glucocorticoids from the adrenal may be implicated in these abortions. Violence and trauma are explanations often relied upon by laymen and veterinarians as an easy way to explain certain abortions when the cause cannot readily be ascertained. If abortion does occur after an injury it is fortuitous and usually not due to the trauma so other causes should be considered.

Genetic or Chromosomal Causes of Abortion

Inbreeding has resulted in increased embryonic deaths, abortions and stillbirths because of a greater concentration of lethal genes per zygote than in crossbreeding. Abortion at term or "stillbirths" were increased with inbreeding in cattle and were associated with posterior presentation, dystocia, malposture of the fetus, twinning and fetal abnormalities.¹⁰ Sixty-two percent of the "stillbirths" were males. The incidence in first-calf heifers was 6.7 percent compared to 2.4 percent of the rest of the cattle. Certain genetic defects of the bovine fetus may result in intrauterine death and abortion such as, fetal anasarca in Ayrshires, osteopetrosis in Angus, and severe achondroplasia in Dexters (See Chapter III).

An incidence of 20 and 45 percent, respectively, of chromosomal anomalies were present in over 300 spon-

taneous abortions in humans.^{1,2,9} About half of these abnormal embryos had an extra chromosome, trisomy; others were monosomic or polyploid. In another study of nearly 40 human couples in which the female partner had a history of habitual abortion, it was shown that most of these men and women did not have demonstrable genetic chromosomal abnormalities and this was not a common cause of recurring abortions.⁷ However, one female heterologous translocation carrier was discovered that was traced through three generations. Impairment of fertility occurred in 3 of the 4 female carriers of this chromosomal defect.

An abnormal diploid chromosome number was reported in the Swedish Red and White breed.⁴ In 1173 animals examined 14 percent were heterozygous with a chromosome number of 59 and 0.34 percent were homozygous with 58. This was caused by a translocation, Robertsonian, between the largest and smallest chromosome pairs. This resulted in a 2 to 3 percent lower conception rate in heterozygous bulls and cows due to an increased incidence of early embryonic deaths. Few reports of similar cases in animals of early embryonic deaths and aborted embryos and fetuses are available. It is probable that a certain percentage of abortions in cattle are due to chromosomal abnormalities. Ten to 12 percent of the blastocysts from normal sows had detectable chromosome defects and this may account for about 30 percent of the total pregnancy wastage which in sows is about 30 to 40 percent of the fertilized ova.⁵ Polyploidy was the most common chromosomal abnormality in those defective zygotes. Tetraploid cells were found in a bovine blastocyst.⁶ Polyspermy associated with delayed insemination of sows may be a factor in causing polyploid embryos. In one Holstein herd abortions and fetal mummification occurred commonly at 120 to 180 days of gestation in daughters of two popular sires when they were mated to the other sire. It was postulated these abortions and mummified fetuses were caused by an autosomal recessive gene carried by the heterozygous sires and dams. When the owner ceased to use these two bulls on each other's daughters the losses stopped.⁸ The genetic aspects of fetal and newborn calf losses has been reviewed.³

Miscellaneous causes of abortion

Twining in cattle, as discussed previously, is associated with a higher rate of premature births, abortions, dystocias and expulsions of dead or weak fetuses at term than occurs with single fetuses. Retained placenta is also common after the birth or abortion of twins. This may be associated with a lack of placental area and

nutrition for the fetuses, uterine inertia or "wedging" of the fetus from each horn into the pelvis at the time of expulsion or possibly other causes. Abortions and fetal loss is more common with unicornual than bicornual twin pregnancies in cattle.

Allergies and "anaphylactic" reactions may cause abortion in cattle. Abortions that followed within 2 to 3 days the anaphylactic reactions observed after using an early leptospiral bacterin containing rabbit serum were described previously. Four cows aborted within two or three days following an allergic reaction due to the intravenous administration of tuberculin.² Urticaria associated with milk allergies in cattle, especially Jerseys and Guernseys, occurring at the time of "drying off" have resulted in abortions and premature births.³ Attempts to produce abortions in cattle as a sequel to an incompatible blood transfusion failed.⁵ However, organisms such as *Alcaligenes fecalis*, *Pseudomonas* and others or their products present in contaminated sodium citrate solution if added to blood at the time of blood collection produced a severe anaphylactoid reaction resembling either an incompatible transfusion reaction, or most likely an endotoxin reaction in transfused cows resulting in abortion several days later. The anticoagulant sodium citrate solution should be made up fresh, just before use, with pyrogen-free sterile water to prevent these untoward transfusion reactions in cattle.

Other miscellaneous abortions have been associated with lymphocytoma in which the uterine wall was extensively involved, in *C. pyogenes* abscesses of the uterine wall, in extensive adhesions of the uterus to the body wall or other viscera limiting uterine enlargement, and in cattle where there is a congenital or acquired lack of most of the uterine caruncles and endometrial glands. Abortion in anemic cattle severely infested with the sucking louse has been reported.^{1,4}

Fetal mummification due to the intrauterine death of the fetus and failure of its expulsion or abortion is due to many of the factors described above that cause bovine abortions. These will be discussed later in this chapter.

A Review of Aids in the Diagnosis of the Cause of Abortion

In order to improve the possibility of making a diagnosis of the actual cause or causes of abortion in cattle the attending veterinarian should secure a very careful, detailed history of the herd and cows involved over the past 6 to 9 months including breeding dates, sires used, whether natural or A.I. service, previous breeding history of the cow or herd, herd health history especially noting any illness in the herd over the past few months,

new arrivals into the herd or possible contacts between the herd and other herds should be noted. The health and reproductive history of the herd of origin of purchased cattle or the contact herd is desirable. The number of abortions and the time in gestation they occurred should be recorded. The freshly expelled fetus and its membranes including the cotyledons and amniotic fluid, if available, should be taken as cleanly as possible and placed in a waterproof plastic bag or clean can and refrigerated and delivered immediately to the diagnostic laboratory. If the fetus is large, a careful necropsy should be performed and specimens of the stomach, tied off at each end, lungs, liver, spleen and kidneys should be saved for culture and gross and histologic examination. These also should be carefully refrigerated and taken immediately to the laboratory along with representative portions of the fetal placenta. Freezing of tissues while good for recovery of most organisms and viruses may interfere with the diagnosis of certain protozoal causes of abortion and with tissue sections and their examination. In an outbreak of abortion it may be necessary to examine 3 or 4 fetuses to find one that may yield clues to the cause of the outbreak. Blood samples from the aborting cows should be taken in a near sterile manner at the time of abortion and then again 2 to 3 weeks later. Samples from other cows in the herd, those acutely ill, representative cows or recently introduced cattle might also be collected for blood testing. The serum from these samples should be removed and saved, even by freezing, if necessary, for serologic determinations. Sending whole blood samples into the laboratory during the hot summer months may result in hemolyzed samples if they become overheated or in the winter if they become frozen. It should be recognized at the present time that because of the multiplicity of causes for bovine abortion, the as yet unknown causes, and the great frequency of partially autolyzed fetuses by the time they are expelled that only about one in three or four, 25 to 30 percent, of aborted bovine fetuses can be accurately diagnosed with respect to the causative agent. Laboratory procedures for the diagnosis of the major infectious causes of bovine abortions have been described.¹⁷

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Bovine Abortion

Infectious Causes—Bacterial

Brucellosis

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ABORTION IN MARES

The incidence of equine abortion is higher than that experienced by cattle and is given as about 10 to 15 percent. About 8 to 10 percent of mares diagnosed pregnant at 40 to 45 days lose their conceptuses by 90 to 100 days and 4 to 6 percent lose fetuses from 100 days to term.^{4,27} Many of these abortions are apparently not associated with infectious agents. A good diagnostic laboratory supplied with fresh, properly-handled, chilled equine fetuses and membranes can usually determine the cause of abortion in 60 to 80 percent of the cases. This is particularly true if there is an enzootic outbreak of abortion on a farm and a number of specimens are examined. Most observed abortions in mares occur after the fourth month of gestation. The diagnosis of most of the causes of early unseen embryonic or early fetal deaths in mares is speculative or unknown. As in other species of animals, equine abortions may be caused by bacterial; viral; fungal; protozoal; chemical, or hormonal; nutritional, physical, genetic or chromosomal and miscellaneous causes. Twinning is a common cause of observed abortion from 5 months to term with a reported incidence of 20 to 30 percent of these late abortions.^{14b,27,31} (See Table 10.)

Infectious Bacterial Abortions in Mares

Evidence would indicate that many of the infectious bacterial organisms causing abortion result from ascending infections through the cervix. Bacterial infections of the placenta and fetus may cause abortion at any stage of gestation.^{2,4,9,11,27,28,31,32} Early abortions from 25 to 150 days are seldom observed especially in mares on pasture. Thus these abortions early in gestation, usually detected by rectal examination, at 20 to 60 days and again at 100 to 150 days are often considered as embryonic or fetal resorptions or infertility of unknown cause. Uterine cultures of mares several months after early fetal loss are usually negative for evidence of infection. However, when some of these early autolyzed fetuses and placentas were examined a variety of pathogenic and contaminating bacteria were present including in a majority of cases a

Table 10. Summary of Causes of Abortion in Mares

Infectious causes

Bacterial-**Streptococcus zooepidemicus**, alpha hemolytic streptococcus, **Salmonella abortus equi** and leptospirosis (**Leptospira pomona** and possibly other leptospira), **Hemophilus equigenitalis** (C.E.M.).

Miscellaneous Bacterial-anaerobic, motile (Lancefield Group D) and other streptococci, **E. coli**, **Pseudomonas aeruginosa**, **Corynebacterium equi**, **Actinobacillus (Shigella) equuli**, **Streptococcus equi**, staphylococci, **Klebsiella**, **Brucella abortus**, mycoplasma, diptheroids, sarcina, **Pasteurella hemolytica**, **Listeria monocytogenes**, **Corynebacterium pseudotuberculosis**, **Acinetobacter calcoaceticus**, and **C. pyogenes**,

Viral-Rhinopneumonitis or Equine herpesvirus I, arteritis virus

Miscellaneous viral-equine infectious anemia virus

Mycotic or fungal-**Aspergillus fumigatus**, Mucorales, **Allescheria boydii**, Histoplasma, **Coccidioides immitis** and the yeasts, **Candida albicans** and cryptococcus

Protozoan-**Trypanosome equiperdum** (dourine), **Babesia equi** and **caballi** (piroplasmiasis), Bedsonia, and Sarcocystis

Noninfectious causes

Chemicals, drugs and poisonous plants (no material or substance confirmed as a cause for equine abortion)

Hormonal-estrogen, prostaglandins, oxytocin(?), progesterone deficiency, and cortisone excess (stress)

Nutritional-reduced energy intake and other stresses.

Physical-manual dilation of the cervix and douching of the uterus, trauma or injury to the very young blastodermic vesicle, torsion and strangulation of the umbilical cord and torsion of the uterus or strangulation of the uterus by a lipoma

Genetic or chromosomal-fetal anomalies, early embryonic deaths

Miscellaneous causes-twinning, early embryonic deaths, early conception after foaling(?), increasing age of mare, and effect of sire on abortion.

microaerophilic, alpha hemolytic **streptococcus spp.** with fastidious growth requirements.³² This organism has also been recovered in cultures of the endometrium and external genitalia. Another preliminary study¹⁶ has confirmed the original observation³² that nonfecal alpha hemolytic streptococci are a cause for early fetal deaths from 45 to 90 days of gestation. This organism when inoculated into the mare's uterus during the estrous period did not cause infertility or early embryonic death.¹⁶ Further studies on this organism and its role in early abortions are indicated.

A possible factor favoring infections of the caudal portions of the genital tract ascending through the cervix in early pregnancy is the high rate, 72 percent and possibly more, of secondary ovulations from 50 to 75 days of gestation with a concurrent relaxation of the cervix.^{1,32} However, it should be noted that from 30 days in gestation the cervix and vagina contain a large amount of heavy, tenacious, thick mucus that acts as a seal to prevent bacterial invasion of the uterus. This natural defense mechanism deserves further study to determine its efficacy. Furthermore, stress factor during early pregnancy in the mare may also result in abortions^{4,22,23,26} with a temporary invasion of the uterus by bacteria from the caudal portions of the tract during the period from fetal death to final expulsion. (See early embryonic deaths in horses.)

Nearly all fetuses and placentas examined and cul-

tured by diagnostic laboratories and reported upon have been 5 through 11 months in gestational age at the time of abortion. There are no venereal diseases of horses, such as campylobacteriosis and trichomoniasis in cattle, causing endometritis and early embryonic deaths except contagious equine metritis (CEM) caused by **Hemophilus equigenitalis** and possibly certain pathogenic strains of *Klebsiella* and *Pseudomonas* which will be discussed in Chapter XIV on Infertility in the Mare. Other bacteria, especially **Streptococcus zooepidemicus**, found in the caudal portions of the genital tract should not be considered as organisms causing a contagious venereal disease.

Streptococcus zooepidemicus (genitalium), a beta hemolytic streptococcus, is the most common bacteria found in genital infections in horses. This organism is a hemolytic streptococcus, Lancefield's Group C, found ubiquitously on the external genital organs of all mares and stallions. It may be cultured from the genital tract for a few days after foaling in about 90 percent or more of mares. It is usually found as a contaminant from the prepuce in the semen of stallions. It is the most common organism associated with metritis, cervicitis, and vaginitis secondary to pneumovagina or "windsucking." Streptococcal abortions are most common on poorly managed farms. By proper management procedures, routine genital examinations and cultures, antibiotic therapy, vulvasuturing, sexual rest, and regulated, supervised hygienic

breeding, almost all mares infected with this organism can be cured and the infection prevented or controlled. This results in a very low incidence of "strep-infected" mares on a well-managed farm. Mares with a lowered resistance, trauma, or disease of the genital tract, mares bred on the ninth day after foaling, mares with lesions of the genital tract and pneumovagina, and old mares with localized areas of dilation of the uterine wall and cystic degeneration of the endometrium are most prone to the establishment of this common infection in the genital tract. The healthy genital tract of normal mares is resistant to infection including *Str. zooepidemicus* commonly introduced at parturition and breeding.

Streptococcus zooepidemicus may cause 10 to 20 percent of abortions especially on poorly managed farms. It has been reported in up to 40 percent of the aborted fetuses infected with bacteria. Since this infection is limited to the genital tract and is not spread by ingestion or other means, abortions occur in chronically-infected mares in a sporadic manner. Streptococcal abortions may occur at any stage of gestation. This organism is a common cause of infertility and early abortion from 2 to 5 months of gestation and infection in newborn and postnatal foals.^{1,3,11} Following streptococcal abortions in the last third to one-half of gestation, retained placentas are frequent and infections of the uterus tend to persist after abortions. Some abortions are preceded by a mucopurulent vaginal discharge.

Aborted fetuses show autolytic changes that vary from slight changes to complete maceration of the fetus. *Streptococcus zooepidemicus* may be recovered from the fetus, the fetal membranes and the genital discharges. There is no serologic test for streptococcal antibodies.

Prevention of abortion due to *Streptococcus zooepidemicus* relies on proper management and the breeding of only normal healthy mares. Barren mares should be culled in the fall of the year and if infected should be given suitable antibiotic and surgical treatment so the infection is overcome before breeding. Proper hygiene in the breeding shed and avoiding frequent copulations may be helpful. Certain older pluriparous mares with a lowered resistance to infection may require local antibiotic therapy after service and/or artificial insemination with semen containing antibiotics. Chapter XIV on Infertility in Mares discusses in detail the diagnosis, therapy and preventive procedures for *Streptococcus zooepidemicus* infection of the mare's genital tract.

Salmonella abortus equi causing contagious equine abortion was first reported in 1893² and studied and described in Kentucky in 1911 where outbreaks were common. This cause of abortion in mares has been reported

in a number of states in the U.S., several European countries, Canada, South Africa, South America, and Japan. *Salmonella* abortion in mares has not been described in the United States since 1932 except for two isolated outbreaks in Illinois and Washington.^{5,6,24} The reason for the near disappearance of this disease is not known. *Salmonella abortus equi* may be carried in the intestinal tract of apparently normal horses. Other *Salmonella* serotypes have not been described as a cause of abortion in mares with the possible exception of *S. anatum*.¹⁵

Salmonella abortus equi is spread by ingestion of feed and water contaminated by feces or genital discharges from aborting mares, especially when horses are on pasture. The incubation period is from 10 to 28 days and just before abortion occurs the mare may exhibit a general reaction, depression, anorexia and fever. If the mare is not observed closely these signs are missed and abortion results without apparent premonitory signs. Retention of the placenta may occasionally follow abortion. Most abortions occur between the 6th and 9th month of gestation but some may occur as early as the 4th month to as late as the 11th month. Infected foals born at term are weak and usually die within several days. In a susceptible band of mares the incidence of abortion may reach 50 to 90 percent. The abortion usually has no effect on the future fertility of the mare unless lacerations or other infections cause subsequent chronic infection of the mare's genital tract.

The allantois chorion of the placenta often shows non-specific edema, necrosis, and hemorrhage. The fetus exhibits autolytic lesions of edema and the presence of reddish serous fluid in the body cavities. The organism may be cultured readily from the fetal organs and tissues, the fetal membranes, and the uterine exudate. Organisms in the uterine discharge disappear rapidly within a few days after abortion. Further diagnostic confirmation can be obtained by the agglutination test on the serum of the aborting mare.

The yearly use of bacterins has been highly successful in immunizing of mares against *Salmonella* infection contracted by ingestion. Mares were vaccinated subcutaneously at 4 months of gestation at weekly intervals with 1 ml, 2 ml, and 2 ml (double strength) bacterin. This procedure was repeated 3 to 4 months later. Isolation, quarantine, and sanitation procedures were helpful in limiting or preventing severe outbreaks of abortion. For the past 25 years vaccination of mares has not been performed in the U.S.

In an outbreak, or preferably before, the mares should be kept in small units or bands isolated from each other. Aborting mares should be isolated from the normal mares.

All fetuses and membranes should be removed and destroyed and the area disinfected. The bacterin is usually used in an outbreak but some mares may abort before immunity has developed.

Leptospirosis due to *L. pomona*, and possibly other leptospiral serotypes **hardjo**, **bratislava** and **icterohemorrhagiae**^{13b} has occasionally been reported as a cause for abortion in mares from the seventh through eleventh month of gestation.^{8,12,13b,c,14,17,29} Although serologic evidence of leptospirosis was reported in 45 percent of 1606 horses in Georgia⁷ and 5 percent of 1346 horses in northeastern United States,³⁰ no reports of abortions were recorded. Acutely infected mares may show a mild systemic reaction with a moderately elevated temperature of 102 to 103° F, slight icterus, anorexia, and depression that lasts for 3 to 4 days. One to 3 weeks later abortions may occur. The aborted fetus may be slightly icteric and show autolysis. The mare will often exhibit a high leptospiral titer of the blood using the MA test at the time of abortion. The blood testing of normal, acutely ill, aborting and recovering mares in an outbreak may aid in diagnosis. A rising titer associated with abortion is highly significant. As in cattle, recovery of the organism from autolysed, aborted equine fetuses, is difficult. Special staining of fetal organ sections and the fluorescent antibody technique is of diagnostic value in leptospiral abortion in mares. Following experimental infection, horses can shed *Leptospira pomona* in the urine for 70 to over 94 days, but less than 120 days.²⁵ Periodic ophthalmia occurred in some of these horses 12 to 14 months later. Treatment of leptospirosis in horses with antibiotics is similar to the treatment in cattle and swine. Yearly vaccination of horses at risk with a bacterin the first trimester of gestation may prevent abortion as well as periodic ophthalmia due to *L. pomona*. Since no leptospiral bacterins are available for horses the bovine bacterin is used. Occasional local reactions to the bacterin may develop. If the early mild signs of acute illness due to leptospirosis are observed including: moderately elevated body temperature, depression, inappetance and slight icterus, the affected animal should be placed on therapeutic levels of streptomycin and penicillin for 4 to 5 days. This therapy during the early stages of the disease may prevent abortion as well as periodic ophthalmia caused by *L. pomona*.

Miscellaneous bacterial infections associated with sporadic abortions in horses may cause from 5 to 10 percent of the total abortions due to bacterial agents.^{2,4,9,11,28,31} These include: anaerobic **Streptococci viridans**, motile **Streptococci** (Lancefield Group D), **Streptococcus equi**, **Staphylococcus aureus**, **Escherichia coli**, **Actinobacillus** (**Shigella**) **equuli**, **Corynebacterium equi**, **Kleb-**

siella spp, **Pseudomonas aeruginosa**, diphtheroids, **sarcina**, **Brucella abortus**,^{10,20,21} **Pasteurella hemolytica**,³³ **Acinetobacter calcoaceticus**,^{13a} **aerobacter agglomerans**,^{13b} **Listeria monocytogenes**,¹⁹ **Corynebacterium pseudotuberculosis**,¹⁸ **Corynebacterium pyogenes**, and mycoplasma.^{16c,3,28} Pure cultures of bacteria from the organs of aborted fetuses is the usual means of diagnosing these sporadic causes of abortion. Many bacterial agents causing abortion may be present in the cervix and uterus at conception and persist for a varying period. Other organisms may ascend through the cervix into the uterus during early pregnancy. While others, such as leptospira and salmonella, gain access to the uterus hematogenously during pregnancy. It is probably uncommon for organisms to enter the uterus through the normal closed and sealed cervix during late pregnancy.

Viral Causes of Abortion in Mares

Abortion in mares is known to be caused by the rhinopneumonitis or **equine herpesvirus I**. Rarely abortions are reported associated with **equine infectious anemia**, **arteritis virus** and other viral diseases.

Abortion due to the **equine herpesvirus I** (EHV1) or **rhinopneumonitis virus**.

Abortion in mares is commonly due to **equine herpesvirus I**. This virus has many similarities in common with the IBR-IPV virus in cattle.²⁹ However, the IBR viral vaccine did not produce antibodies or heterotypic immunity to equine herpesvirus in horses. Other herpesviruses have been isolated from horses.³⁶ These include equine herpesvirus 2 (or equine cytomegalovirus), and equine herpesvirus 3 (or equine coital exanthema virus). The former ubiquitous virus that persists in a horse for long periods, has been associated with some forms of respiratory disease and the latter virus causes an acute mild venereal disease characterized by pustular lesions on the vaginal and vestibular mucosa and skin of the perineal region of mares and the modified skin of the penis and prepuce. Neither of these latter two viruses, EHV2 or EHV3 cause abortion.^{2,4,22,36}

Virus abortion was prevalent in Kentucky at least as early as 1922. It was shown to be caused by a virus in 1936.¹¹ In 1941 it was reported that equine virus abortion was secondary to influenza. In 1954 Kentucky researchers^{11,17} demonstrated that the virus of equine virus abortion and equine "influenza" virus were the same. Since then two true influenza viruses, Prague, A₁ and Miami, A₂, have been isolated, so the name rhinopneumonitis and then equine herpesvirus I was given to the herpes virus causing an upper respiratory disease in horses

and abortion in mares. The incidence of herpesvirus abortions in Kentucky varied from 4 to 26 per thousand broodmares with an average of 10/1000 or 1 percent from 1957 to 1977.⁴

Rhinopneumonitis, abortion and neurologic disease or paralysis due to equine herpesvirus I have been commonly diagnosed in Europe, Japan, Canada, Australia, and the U.S.^{1,2,2,8,9,16,19,23,24,36} The respiratory form of the disease is very common; the abortigenic form is less common. The neurologic form which occasionally follows the respiratory or abortigenic forms is uncommon or rare. The disease may be introduced into a farm by infected foals or horses and by infective material carried by persons, dogs, foxes, or carrion birds. This virus is quite resistant and may survive 7 to 42 days or more in dry stable surroundings.¹⁴ Following a natural infection the horse may spread the virus for 3 to 4 weeks. This virus, as other herpesviruses, may persist or be latent in certain tissues of "carrier" animals for long periods of time. Stress probably plays a role in releasing this virus and causing an exacerbation of the disease. Equine herpesvirus I is only naturally pathogenic for horses. It can be adapted and grown in suckling hamsters and in cultures of kidney tissue cells from a number of animal species.

Recent studies^{19,24,36,37,39} on respiratory and abortigenic strains or subtypes of equine herpesvirus (EHV) I using restriction endonucleases to analyse the DNA of the virus have shown them to be dissimilar. Based on this and clinical, serological and laboratory observed differences in the strains^{24,36,37,39} it was suggested that further studies on the various subtypes and vaccine effectiveness are indicated.

The clinical signs of rhinopneumonitis are those of a mild, febrile respiratory disease usually observed in young horses 4 to 8 months of age in the fall and early winter months. The incubation period is 2 to 3 days. The body temperature is elevated to 102 to 104° F. A serous rhinitis with congestion of the nasal mucosa and conjunctiva occurs often associated with coughing, inappetence, and depression. A leucopenia usually is present. In about 7 to 10 days, the febrile period ends and a mucopurulent rhinitis, "the snots," develops which, along with a cough, lasts for several weeks or longer. The disease can occur in any age of horse at any time of the year. The virus is highly infectious and contagious and is spread mainly by inhalation or droplet infection or occasionally by ingestion. In older mares this disease may frequently be so mild as to be unrecognized.

The incubation period for abortion in natural infections due to rhinopneumonitis virus or equine herpesvirus I is 20 to 30 days with a range of 14 to 120 days.^{13,36}

Since evidence indicates that fetuses die soon after they are infected with herpesvirus I and are aborted, the long incubation period of this disease is intriguing. It has been shown that a viremia with the virus in the lymphocytes and monocytes^{2,3,4,21} may last for about 21 days. It has been hypothesized that the virus may reside in the chorion of the placenta for a time, as is possible with IBR virus in cattle, before infecting and rapidly killing the fetus.²⁶ Thus abortions in mares on breeding farms often follow the outbreak of the respiratory disease in foals by several months.¹⁶ If the mare exhibits typical respiratory signs of the disease, abortions may follow apparent recovery by several weeks or months. Fetal deaths and abortions seldom occur before 5 months of gestation and over 90 percent of the abortions occur from 8 to 11 months of gestation. Often foals infected in utero may be born alive but die within a few minutes to 4 days postpartum. Some workers consider this neonatal EHV I infection, associated with a high mortality rate from respiratory failure, a fourth form of the disease.^{5,10} Live foals infected with EHV I virus before birth often have an elevated temperature, heart rate and respiratory rate, edema and congestion of the lungs and a leucopenia. Thus breeding practices largely determine the season or time when abortions occur; in Kentucky 90 percent of the abortions occurred from December through April.

Immunity to herpesvirus (EHV) I, like other herpesviruses, is relatively short lasting only a few months to a year and requiring frequent natural exposure or vaccination to maintain protective antibody levels in the blood.^{1,2,3,4,14,30,36} The degree of immunity and the number of pregnant mares at the time of the outbreak determine the abortion rate on a farm which may vary from 1 to 90 percent of a band of mares. Keeping the pregnant mares on a farm separated into small units well-isolated from other mares, horses, and young stock does much to reduce the spread and incidence of abortion in an outbreak. In Kentucky 85 percent of the farms had 3 or fewer cases of virus abortion with an average abortion rate per farm per year of 2.5 percent, with a range of 1.6 to 6 percent. Abortions on a farm will occur over a period of 2 weeks to 3 months with 88 percent of the abortions occurring within 60 days of the first abortion. Data from Kentucky in 1963 indicated that this virus was present in 52 percent of aborted, infected fetuses and caused 26 percent of the total abortions in mares.¹⁶

The equine herpesvirus I causes the death of the fetus and no signs of impending abortion are observed. Retention of the placenta is uncommon. The mare is not traumatized unless a large fetus causes tearing of the tissues of the vulva or perineal region. Following viral abortions, mares usually conceive readily the next breed-

ing period unless secondary infections have occurred.^{1,2,8,16,33}

Examination of the aborted fetus and membranes in this disease usually reveals a "fresh" nonautolyzed fetus, an edematous amnion, yellow amniotic fluid, a slightly yellow or icteric color of the fetal body tissues, straw-colored fluid in the thoracic cavity, interlobular edema and small hemorrhages in the lung, petechial and ecchymotic hemorrhages in the epicardium, and small whitish-yellow, pinhead-sized foci of necrosis in the liver. On microscopic examination of stained liver, bile duct, lymph node, thymus, and bronchial cells, intranuclear inclusion bodies are frequently found. These latter signs in the fetus are of great diagnostic value. (See Figures 67 and 68.)

The neurologic form of herpesvirus I may follow or occur with abortion in pregnant mares or after the onset of the respiratory form of the disease when EHV I invades the central nervous system producing disseminated, necrotizing myelo- and meningo-encephalitis with vasculitis of the smaller vessels of the brain and spinal cord. The clinical signs vary from a mild ataxia to complete paralysis and death.²⁵ In recent years this form of the disease has been reported widely in a number of states in the United States, Canada, Europe and Australia. Some of these reports described cases of epizootic outbreaks of the neurologic disease.^{10,23,27} A number of cases followed about 10 days after the vaccination of horses with a MLV herpesvirus I vaccine grown in a vero-monkey tissue cell line.^{20,28} Although this commercial product had undergone extensive trials prior to approval, it was withdrawn from the market because of its propensity to rarely produce neurologic disease. Treatment of this neurologic



Figure 67. Liver and lung of an aborted 10-month equine fetus. Fetal death was due to equine herpesvirus I. Note small necrotic foci in the liver and edema of the lung. (Courtesy K. McEntee.)

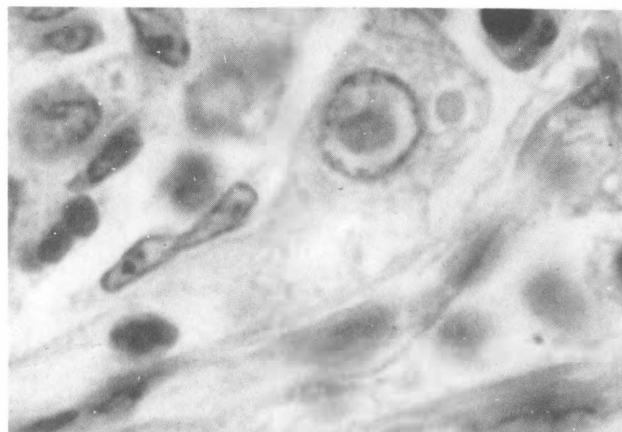


Figure 68. Intranuclear inclusion body in a liver cell of an equine fetus following herpesvirus abortion. (Courtesy K. McEntee.)

syndrome is entirely by supportive therapy and deaths are common.³⁵

There is no permanent immunity to viral rhinopneumonitis or abortion. Many aborting mares apparently develop a fairly long immunity of one to two years. The respiratory form of the disease does not provide as long nor as good an immunity as occurs following an abortion. Some horses may lose their immunity within 3 to 6 months after infection or vaccination but the disease is so common that most horses are frequently exposed and thus maintain a satisfactory immunity. Repeated frequent exposures to diseased horses or repeated vaccinations with a vaccine increases the level of resistance. Strict isolation of mares on breeding farms without vaccination is therefore likely to increase their susceptibility.

The complement fixation (CF) test or serum neutralization test can be used to determine antibody levels in the serum of horses following this viral respiratory disease or abortion but it is not diagnostic. Antibodies persist for only a month or two up to one year even in aborting mares.^{3,14,16} This test is also of limited value in diagnosis since both CF positive and negative mares may abort or not abort when challenged by the equine herpesvirus I. During and after a respiratory infection or exposure to virus from an abortion, there is a viremia persisting for up to 3 weeks in mares despite the coexistence of virus neutralizing antibody in the blood.³ The virus is carried within the lymphocytes and the latter cells carry the virus throughout the body and to the placenta. It was shown that several "grades" of immunity existed depending upon the amount of antibody present at the site of infection in the nasopharynx. This immunity was a reflection of the level of virus neutralizing antibody in



Figure 69. Torsion of the umbilical cord of a 7-month equine fetus resulting in abortion.

the blood.^{2,3,4,12,30} Culture of the liver or lungs of freshly aborted fetuses on tissue culture medium often results in the recovery of the virus. The fluorescent antibody test applied to fetal tissues also is of great diagnostic value.³⁴

Although many small horse farms with multiple equine activities experience a constant influx of "outside" horses and a constant exposure of broodmares to infection with EHV I virus, they seldom experience a serious epizootic outbreak of virus abortion. However, in controlling herpesvirus I infection on a large breeding farm certain management procedures should be considered. Outside horses, especially from sales, should be carefully isolated for a month or more as virus may be shed from the respiratory tract and the horse appear clinically normal. Furthermore, if the addition to the farm is a mare in the

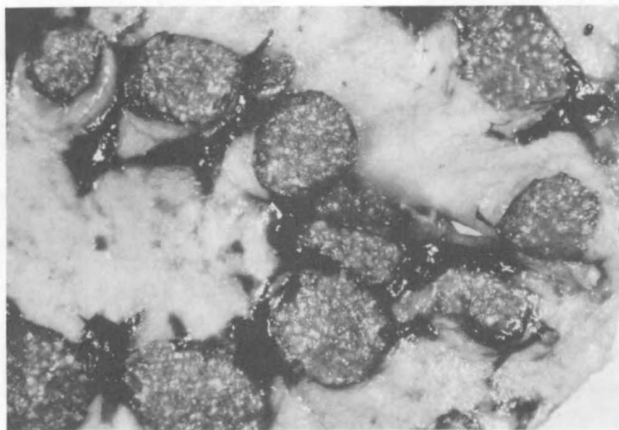


Figure 70. *Toxoplasma gondii* abortion in a ewe. Note the white toxoplasma bodies in the maternal caruncles.

latter half of gestation, isolation should be longer since the incubation period for abortion may be up to 4 months. Pregnant mares should be handled to avoid stress. Mares should be placed in small bands and not changed around. These bands should be kept separate from each other. Foals on nursing mares should be weaned early in a manner to avoid stress on the mare and to keep foals with the commonly occurring herpesvirus respiratory disease separated from the broodmares during the late fall and early winter. Pregnant mares in the last trimester of gestation should be kept from exposure to EHV I virus during this critical period. Since vaccination does not protect all broodmares, management procedures to reduce stress and prevent the spread of the disease should be instituted.^{1,4,19}

Since 1950 various vaccination procedures have been developed and discarded as better ones have superseded them. Initially a vaccine was prepared from equine fetal tissues.¹⁸ This killed vaccine which contained some red blood cells produced isoantibodies in some mares resulting in neonatal isoerythrolysis in their foals. The next vaccine was prepared from hamster tissues containing a live virulent virus that was injected intranasally.^{12,14,15} This product was not satisfactory for use on farms with a long breeding season as this vaccine produced a "controlled" or "planned" infection that could spread to other horses and it required that all horses on a farm be vaccinated at the same time and "quarantined" for 3 to 4 weeks.

In recent years two other vaccines have been developed. One, a modified live virus (M.L.V.) vaccine that is given in two doses 4 to 8 weeks apart in pregnant mares after the second month of pregnancy and repeated every six months. Since immunity is rather short-lived repeated vaccinations are necessary to maintain high levels of antibody in the blood. This vaccine does not cause abortion or respiratory disease and does not spread to susceptible horses.¹ The other vaccine is an inactivated EHV I vaccine with an added adjuvant that is recommended for use in pregnant mares at 5, 7 and 9 months of gestation to maintain a high level of protective antibody.⁴ Both of these latter vaccines apparently provide a significant protection against abortion due to EHV I. However, a few vaccinated mares if stressed and/or exposed to a severe challenge with virulent virus may abort.^{1,4,19} Of 8638 pregnant mares vaccinated from 1977 through 1980 with the inactivated vaccine, 1.6 per thousand aborted compared to 6.8 per thousand in 20,732 nonvaccinated mares.^{4,39} Of 233 abortions in vaccinated mares during a five year period a field strain EHV I was isolated from 93 fetuses. For this reason claims for its effectiveness in protecting pregnant mares from abortion

have been largely omitted. However, serological and clinical protection on two horse farms indicated the MLV vaccines probably are of value when used every 3 to 4 months.^{4,30} If an abortion due to EHV I occurs in a band of broodmares, prompt vaccination of all unvaccinated or susceptible mares is indicated to cause a rapid rise in levels of antibody in the blood. Adverse local reactions such as abscesses may rarely occur following the use of vaccines.⁴

One study indicated it was extremely difficult to evaluate the efficacy of vaccines in preventing EHV I abortion because of the paucity of non-exposed mares, the lack of tests to measure residual protection and an incomplete understanding of the pathogenesis of the disease.²¹ Further studies on the development of vaccines against the strains of EHV I, respiratory and fetal, are indicated.^{24,36,37,38,39}

Since vaccination at present is not completely effective in the control of abortion due to EHV I, sound management procedures should be combined with vaccination to control this disease.

Equine viral arteritis (EVA) or epizootic cellulitis-pinkeye syndrome is caused by the arteritis virus, a togavirus, Bucyrus strain,² that produces signs of severe general respiratory disease including abortion. These signs are closely related to the constant and characteristic necrotic lesions in the media of the small arteries produced by the arteritis virus and causing edema, hemorrhages, and infarcts. The disease is usually brought to a farm by an infected or convalescent horse. Outbreaks are presently very infrequent in the U.S. The disease has been described in Europe.² The virus is spread by droplet or aerosol infection and contracted in inhalation. Thus close contact between horses is necessary for the spread of this disease. The horse is apparently the only natural host of the disease. Since a carrier state can exist, spread of this disease at the time of coitus may occur.¹²

Clinical signs of the disease are often severe and should not be confused with the milder "shipping fever" type diseases of influenza or rhinopneumonitis.^{1,2,6,9,10} Horses of all ages may be affected. The incubation period of the disease is 3 to 9 days. The signs of the disease often include: an elevation of the body temperature to 103 to 106° F; leucopenia with panlymphopenia; conjunctivitis, lacrimation and occasionally keratitis, photophobia and palpebral edema; severe depression; a serous nasal discharge and congested nasal mucous membranes; an increased respiratory rate of 30 to 50 per minute, and occasionally dyspnea with a "heave line"; generalized weakness and stiffness; anorexia; a rapid loss of weight; and frequently colic and diarrhea. In a few horses edema of the limbs and/or the ventral abdominal wall develops.

The course of the disease is 2 to 15 days. Deaths in natural outbreaks are not common but experimentally infected old horses, pregnant mares, and weanlings may develop a severe illness with a 30 to 50 percent mortality due to pulmonary edema, pleural effusion, and secondary cardiac disturbances. However, some natural cases of the disease may be so mild the signs of illness may pass unnoticed.

Abortions are closely associated with the febrile and early convalescent period of the disease and occur 1 to 14 days after the onset of signs of illness. The mare fails to show signs of impending abortion. Abortion may occur in up to 50 percent of the pregnant susceptible mares exposed to the virus.^{2,8,9} Some mares abort without obvious signs of clinical illness and some mares with definite signs of illness will not abort. Most abortions occur in mares from the fifth through tenth month of gestation. Retention of the placenta is uncommon in aborting mares. Some fetuses apparently die 2 to 4 days before abortion because autolytic changes are common in contrast to the freshly aborted fetuses associated with rhinopneumonitis virus (EHV-I) infection.² Postmortem fetal lesions include petechial hemorrhages on the peritoneal and pleural surfaces, epicardium and endocardium, and pleural effusions. These lesions indicated viral induced fetal death was followed by abortion. No inclusion bodies are found with this disease but the virus can be recovered from many fetal tissues including the liver and lungs.^{3,16} The virus can be grown on tissue cultures of horse and hamster kidney cells.^{3,15,16} Complement fixation and serum neutralization tests have been developed to detect antibodies.⁵

Following recovery a prolonged immunity to arteritis virus is probable. An attenuated live virus vaccine has been prepared that is an effective preventative.^{7,11,13} This has not yet become available commercially, because of the very limited occurrence of the disease. About 20 years after the severe epizootic outbreaks of viral arteritis on Standardbred farms in the Midwest, a serologic survey in 1972 revealed 55 percent of Standardbreds, 25 percent of a limited number of Saddle-breds and only 1.6 percent of Thoroughbred horses in the United States had positive titers for arteritis virus. An incidence of 2 to 5 percent positive titers were present in horses in England and Switzerland.¹² Thus an apparent subclinical infection was present that conferred a lifetime immunity that resisted challenge with a virulent virus. However, it is evident that Thoroughbred horses in the U.S., England and Japan because of a very low incidence of antibodies are at risk of a serious and widespread epizootic outbreak of viral arteritis should a virulent strain appear. Only 0.3 percent of 3772 horses tested by the National Veterinary

Services Laboratory in 1978 and 1979 were seropositive for EVA.⁶ Proper segregation, isolation, and quarantine along with other sanitary procedures and with prompt vaccination, would be indicated in preventing the spread of this infection on a farm.

Equine infectious anemia is occasionally characterized by abortion in infected pregnant mares.^{2,1,2} The pathogenesis of abortion due to equine infectious anemia virus has not been established and more study is indicated.

Mycotic or fungal agents of the species *Aspergillus fumigatus*, the order *Mucorales* and *Allescheria boydii*, may cause sporadic abortions in mares. Occasional cases of yeast abortion due to *Candida albicans*¹ or *cryptococcus*^{7b} as well as rare cases of abortions due to histoplasma² and coccidiomycosis due to *Coccidioides immitis* have been reported.⁶ Mycotic agents may cause 5 to 10 percent of all abortions in mares in central Kentucky. Mycotic abortion has also been reported in Germany and England.^{1,3,4,5,7} The cause of the abortion is apparently a severely diseased necrotic, thickened allantois chorion which interferes with fetal nutrition and causes growth retardation and fetal death. (See Figure 64.) Mold may be cultured from the placenta, and occasionally the fetal organs such as liver, stomach, lungs and the fetal skin. It is likely that the mold is carried to the placenta in the blood stream from lesions in the wall of the intestine or lungs. It may also be associated, as in cattle, with the ingestion or inhalation of mold spores from moldy hay or straw during pregnancy. Because of the excellent equine uterine defense mechanism, it seems very unlikely that mold introduced into the uterus at the time of copulation would remain viable for months and then infect the placenta. It is possible that fungi could invade the uterus and placenta through the cervix around the second month of pregnancy as described under bacterial causes of abortion. Mold abortions usually occur from the 4th to 11th month of gestation. Following abortion the mold infection does not persist in the uterus but service on the foal estrum should be avoided.

Parasitic protozoan organisms including *Trypanosome equiperdum* causing dourine,^{1,2} *Babesia equi* and *caballi* causing piroplasmosis,⁸ *Bedsonia spp.*,⁷ and *Sarcocystis*³ spp may occasionally or rarely produce abortion in mares. Dourine is transmitted almost entirely by sexual contact. It was first recognized in the U.S. in Illinois in 1885 by W. L. Williams in horses bred to a stallion shipped from France. By use of the complement-fixation test and destroying all reactors the disease has probably been eradicated from the last infected area in southwest U.S. This disease is discussed in more detail in a later chapter.

Babesiosis or piroplasmosis may result in abortion in severely affected horses.^{1,6,8,10} This disease has been reported in South Africa and is endemic in many tropical countries. At present in the U.S. it is limited mainly to Florida. Signs of the disease closely resemble those of equine infectious anemia except icterus and hemoglobinuria may also be present. The parasite is spread by bloodsucking ticks and it may be found, for diagnostic purposes, within the erythrocytes by proper staining techniques. In infected, aborted, premature or term fetuses or foals, icterus and anemia is present requiring differentiation from equine infectious anemia, rhinopneumonitis virus abortion, neonatal isoerythrolysis, and leptospirosis.^{9,10} Abortion may be due to fetal or maternal stress with cortisol production. The fluorescent antibody technique may be helpful in detecting the parasite in the red blood cells of the fetus or foal.⁵ The complement-fixation test on horse serum is highly specific for *B. caballi* infection and blood titers persist for 1 to 5 years.⁴ Therapy for mares with piroplasmosis is available and effective.^{1,9}

Noninfectious Causes for Equine Abortion

Chemicals, drugs and poisonous plants including: phenothiazine; thiabendazole; "Lentin"; purgatives, such as arecoline, aloes; sudan or sorghum pastures,^{34,37} organic phosphate insecticides and anthelmintics; ergot, locoweed (astragalus)^{22a} and others have been reported as possibly causing abortions if given to or ingested by mares in advanced pregnancy. Iodine when fed greatly in excess of normal requirements to pregnant mares for a number of months caused hyperplastic thyroid glands, weak legs and premature birth of moribund foals.¹⁰ Such causes of sporadic abortions are often proposed but the scientific basis for these reports have not been adequately substantiated. If abortion should follow the administration or ingestion of these or other possibly toxic materials the attending veterinarian should obtain a careful history and have the fetus(es) necropsied and examined carefully for the more common, known causes of abortion in horses.

Hormonal causes of abortion in horses have received limited study.

Estrogens in large doses over a long period regularly produces abortion in other species of animals. In mares evidence is lacking for an abortifacient effect of estrogens. One report indicated that estrogen implants of 50 to 150 mg caused abortion in one of 3 mares.³⁹ Further studies are indicated.

Oxytocin or pituitrin administered to pregnant mares prior to 310 days of gestation has not been proven to cause abortion. Oxytocin may induce parturition in mares after 345 days of gestation. Induction of equine parturition will be discussed in Chapter VI.

When pregnant ponies were injected with **human chorionic gonadotropin (HCG)** at a dose level of 2000 I.U. every other day for 3 doses before 39 days of gestation, abortion resulted. Whereas pregnant ponies similarly injected from 40 to 97 days of gestation did not abort.¹

Prostaglandin, PGF_{2a} or one of its analogues, if injected in a single luteolytic dose before 38 days of gestation will regularly cause abortion within 2 to 5 days.^{14,36} A single large dose of P.G.F._{2a} injected into pony mares 70 to 300 days of gestation failed to cause abortion. When repeated doses of 2.5 mg. PGF_{2a} were given at 12 to 24 hour intervals for an average of 3.7 doses all 13 mares aborted within 4 to 5 days, average 38+ hours.⁹ However PMSG remained elevated after abortion in those mares having elevated levels before treatment. Although luteolysis occurred subsequent estrus and ovulation was erratic and generally occurred only after a prolonged interval in mares over 40 days pregnant at the time of treatment. In another trial about 1 mg/45 kg. (10 mg./1000 lbs) PGF_{2a} was given daily to 25 mares pregnant 100 to 245 days. Abortion occurred in 76 percent of the mares within 3 to 6 days and in the others the second through fourth week.¹⁴ Dystocia occurred in one mare. In an experiment with **Equimate** (fluprostenol-ICI) a single 250 µg. injection produced abortions in 2 to 3 days in 7 of 8 mares pregnant 35 days.³⁶ Repeated injections of a similar dose at 12 to 24 hour intervals was necessary to produce abortion at 70 days of gestation. The interval from abortion to first estrus averaged 11 days in mares aborted at 35 days of gestation and 35 to 45 or more days in those mares aborted at 70 days of gestation. None of the former and 75 percent of the latter had an anovulatory estrus prior to an ovulatory estrus following abortion. Apparently if mares abort from 40 to 110 days of gestation when the endometrial cups are present, these structures must involute before normal reproductive cycling is reestablished. For these reasons breeding mares aborted after 40 days within the same year was very difficult.

A **deficiency of progesterone** has been suspected and diagnosed by veterinary practitioners as a cause of abortions from 1-1/2 to 8 months of gestation for the last 20 years based on clinical observations. The primary corpus luteum of pregnancy, along with secondary or accessory corpora lutea developing the first 60 to 90 days of gestation maintain pregnancy until the fourth to fifth month of pregnancy when the placenta, and probably the

fetal gonads, produce sufficient steroids and progestogens to maintain pregnancy to term. After the third to fifth month of gestation the ovaries and corpora lutea involute and have no role in pregnancy maintenance. (See Chapter IV.)

As mentioned previously, many veterinarians have reported an incidence of about 15 percent abortion rate in mares between pregnancy diagnosis at 40 days of gestation and term with two-thirds of that pregnancy loss between 40 and 150 days. Many of these early abortions occur without being seen, often in mares with a history of recurrent or "habitual" abortion. Since most of these aborted fetuses and placentas when examined are negative for evidence of infection or teratologic defects it is logical to possibly suspect a hormonal cause for this high incidence of abortion.

Whether a progesterone deficiency is actually a reason for abortion in the mare is still uncertain.¹⁵ However exogenous supplemental progesterone produces no adverse effects, and has apparently resulted in many abortion-prone mares successfully completing their pregnancy. It has been demonstrated that about 3 to 4 ng/ml or more of progesterone in plasma is necessary to maintain pregnancy.^{14,15,16,36} Daily injections of 200 mg. of progesterone in oil or weekly injections 1000 to 2000 mg. of respositol progesterone resulted in plasma progesterone levels of 2 and 2.5 to 4.5 ng/ml, respectively in ovariectomized mares.¹⁵ In another study pregnant mares were given either 250 mg. progesterone-in-oil or respositol progesterone intramuscularly on day 255 or 270 of gestation. Plasma progesterone levels peaked at 6.5 to 7.2 ng/ml in 6 hours and receded slowly to preinjection levels of 3.4 ng/ml 6 to 8 days later.⁸ These workers recommended injections of 250 mg progesterone in oil every 2 to 3 days or the same dose of respositol progesterone daily to maintain plasma levels of 1 to 2 ng/ml in progesterone-deficient mares.

Administering 22 and 44 mg. of allyl trenbolone orally daily or injecting 1000 mg of respositol progesterone every four days maintained pregnancy in nearly all mares in 3 groups of 8 mares each that were diagnosed pregnant at 30 days of gestation and ovariectomized on days 34 and 35. All eight control mares, 7 of 8 mares given 500 mg. respositol progesterone every 4 days and 3 of 8 mares given 250 mg. of progesterone in oil every two days aborted 4 to 9 days after ovariectomy when the progesterone levels in their blood plasma fell below 2 mg/ml.^{36b} It should be noted that these mares were ovariectomized before placental progestogens were produced.

Since pregnant mares would be producing their own progestogens, the supplemental doses needed to maintain pregnancy might well be somewhat lower than the

above. Possibly they need not be as high 500 mg. progesterone-in-oil given every 48 hours as recommended in a third study.¹² When injections of progesterone are given regularly there is an accumulative effect on the maintenance of high plasma progesterone levels.^{12,16} Further detailed, long-term studies on possible progesterone deficiencies in abortion-prone mares are indicated.

The author has experienced three unusual, recent clinical cases to illustrate the value of supplemental progesterone injections to prevent abortions in mares. One has been reported;^{33a} the two others^{33b} were very similar to the former. These were Thoroughbred mares 7 to 8 months pregnant. One had a history of being barren for several years and aborting twins the year previously. They were observed to suddenly be dripping milk from their udders and showing marked relaxation of their vulva and perineal region indicating impending abortion, possibly associated with twinning. The mares were confined and placed on antibiotics and supplemental progesterone injections of 200 to 500 mg. of progesterone in oil daily for several days followed in one mare by 500 mg repositol progesterone every 3 to 5 days for a month and in the other mare with 200 to 300 mg. of progesterone in oil daily for 14 days. After 10 days these mares were examined, the udder had involuted and the perineal region was no longer relaxed and edematous. In one mare the vaginal mucus was blood-tinged but the cervix was tightly closed in all mares. Rectal examination revealed a live 7 to 8 month-old fetus in each mare. These mares were given 500 mg. of repositol progesterone intramuscularly weekly until 330 days of gestation. These mares each delivered a live but small, 50–60 lb. foal together with a mummified, slightly macerated fetus enclosed in a necrotic, yellowish placenta. The mares and their foals recovered uneventfully. In the three cases impending abortion was “triggered” by the death of one fetus located in one horn based on the examination of the three placentas at birth. The normal placenta and fetus occupied the other horn and the body of the uterus. It appeared evident that the progesterone administered prevented the abortive process possibly occasioned by the release of cortisone or the release of prostaglandin by the dying fetus, the fetal membranes or endometrium. Possibly with the death of the fetus, the deficiency of placental progestagens from that “dead” placenta dropped the progestogen levels low enough to initiate expulsion of the fetuses or all three factors might have combined to initiate the near abortions. Studies of the blood levels of hormones in such cases would be most informative.

A further observation on the value of progesterone in preventing abortion in the “abortion-prone,” nervous mare

is that progesterone therapy in mares, stallions, cats and other animals apparently has a “tranquilizing” and calming effect. This is most noticeable in pregnant animals the latter half of gestation. Thus progesterone therapy may minimize stressful influences that induce cortisone production in the pregnant animal.

Excess cortisone levels induced by stress on the dams or by the exogenous injection of cortisone into pregnant mares requires further investigation. In other species of animals such as cows and ewes cortisone injections or stress particularly late in gestation readily induces abortion or premature birth. Hillman¹⁷ reviewed studies on the effect of cortisone (dexamethasone) in pregnant mares and concluded that induction of abortion early or birth late in gestation even with large daily doses of 10 to 80 mg usually failed. At 320 to 325 days of gestation massive doses of 100 mg. of dexamethasone daily for 3 to 7 days were required to induce foaling. This may reflect the much higher threshold for hormonal effects required in mares compared to other domestic animals.

Despite the above evidence of the lack of the effect of cortisone on pregnant mares, strong clinical evidence cited by Mitchell^{24,25} and Osborne²⁹ and observed by the author³² and other practitioners would indicate that transportation, physical, nutritional or “emotional” stress in certain pregnant mares is definitely related to abortion at any stage of gestation. On horse farms where pregnant mares were used to collect urine as a source of estrogen, 87.3 percent of 237 abortions occurred between 90 to 150 days of gestation and 89 percent of these abortions occurred within 28 days after removing the mares from pasture and stabling them under stressful conditions.²⁵ No infectious agents could be found in these fetuses. By instituting improved management practices the incidence of abortion could be greatly reduced. In another experiment 44 percent of 95 yearlings and two-year-old mares aborted between 30 and 160 days of gestation possibly due to immaturity, inadequate nutrition and physical stress²⁴ as the fetuses on examination and culture failed to show any infectious agents.

Besides the 5 abortions in 6 mares 4 to 5 months pregnant subjected to stress in shipment from New Mexico to New York State cited in the second edition of this book, the author has observed a number of other similar occurrences. Most notable was a stakes-quality nervous Thoroughbred mare with a history of 8 abortions from 2 to 7 months of gestation over the prior 8 years. Culture and biopsy of the uterus were negative and no reason for the recurrent abortions was found. Before breeding she was vaccinated, wormed and had her teeth checked and feet trimmed. The mare conceived readily; was placed in a paddock on the farm with another old nonpregnant

mare for company and was not handled, treated, or removed from the paddock. Ten and one-half months later she delivered a live, normal foal.

Osborne²⁹ observed a 50 percent abortion rate in pregnant mares at all stages of gestation when stressed in shipment to an abattoir where a postmortem survey on 5198 fetuses was performed. Early embryonic resorption was reported in many mares in South Africa that was apparently caused by a severe nutritional stress of the mares³⁸ 7 to 10 days after being placed on poor pasture at 18 days of gestation. Even in other species excessive stress or handling of normal pregnant females greatly decreases the chance for survival of their offspring. Free-ranging female monkeys had a 2.7 percent incidence of stillbirths, caged monkeys a 15 percent and captured wild monkeys brought to the United States a 50 percent incidence of stillbirths.¹⁰⁰ Modern practices of transportation, changes in feeding and environment, thermal and physical stresses frequently imposed on pregnant mares may have a definite influence on the increased incidence of embryonic and fetal deaths and abortions recorded in recent years, especially in racing and show mares.

Nutritional deficiencies as causes for abortion in mares have been reported.^{13,14,19} Many early embryonic deaths occurred 7 to 10 days after the mares were placed on poor pasture at 18 days of gestation.¹⁹ A high incidence of abortion resulted at 3 to 5 months of gestation in mares 1 to 14 days after confinement in barns and the feeding of a poor ration together with a reduced water intake.^{13,14} These early embryonic and fetal deaths although associated with a lowered level of nutrition may have been due to other hormonal or physiological factors previously discussed. There are no authoritative reports on abortions due to vitamin or mineral deficiencies in horses.

Physical causes for abortion in mares

The **manual dilation of the cervix** and the introduction of several hundred milliliters of physiological saline, dilute Lugol's solution or iodized oil readily produces abortion within 3 to 10 days in most mares. Occasionally a second treatment may be necessary.^{17,21} Purposely aborting mares the last 3 months of gestation is not recommended because complications may arise due to the large size of the fetus.

Natural service during early pregnancy, especially the first 3 months of gestation, is not uncommon due to increased ovarian follicular activity during this period. Abortions following natural matings during pregnancy are rare. Artificial insemination with intrauterine deposition of semen causes abortion during early pregnancy.

Trauma or injury has been reported as a cause of abortion in mares. These reports are not well-docu-

mented. Rough manipulation of the blastodermic or chorionic vesicle per rectum from 20 to 50 days of gestation should be avoided. Rectal palpation of the chorionic vesicle for pregnancy diagnosis should be performed carefully and gently to prevent injury. Frequent rectal palpation of 27 mares between 20 and 82 days of gestation caused no abortions.²¹ Only 2 of 6 mares aborted after 145 days of gestation when exposed to severe rectal and vaginal mechanical and thermal irritation. Thus a normal pregnant mare is relatively resistant to abortion produced by physical means. In twin pregnancy diagnosed prior to 30 days of gestation manual destruction of one blastodermic vesicle permitted the other to develop normally.^{7,11b,22} Severe stress produced by prolonged difficult shipping, hard, sustained work, difficult and complicated operations, vigorous struggling and trauma during casting may cause abortion in mares as discussed previously.

Placental insufficiency due to body pregnancies with little or no extension of the placenta into the uterine horns, adhesions or strictures limiting the size of the uterine lumen or access of the placenta to a portion of the uterine horns and extensive areas of chronic endometrial fibrosis may rarely cause abortion.^{20b}

Torsion or strangulation of the umbilical cord is responsible for about one-half to one percent of the equine fetal deaths and abortions from 150 to 300 days of gestation.^{1,5,20} The equine amniotic sac and fetus float free within the allantoic cavity except for the umbilical cord. The long, 55 cm. (range 30 to 95 cm.) umbilical cord in the normal foal has from 1 to 3 rotations.²⁰ In occasional fetuses the cord becomes excessively twisted, swollen and edematous (See Figure 69) or rarely becomes wrapped tightly around a fetal extremity closing the lumen of the blood vessels between the placenta and the fetus. A long umbilical cord may be associated with ischemic necrosis of the cervical pole of the chorioallantois.²⁰ This appears to be accidental. Most of the excessive twisting and vascular occlusion occurs in the amniotic portion of the cord. Strangulation of the uterus by a lipoma or torsion of the uterus may rarely cause fetal death.

Genetic or chromosomal and other causes of abortion

Fetal anomalies as a possible cause for mid to full term equine abortion have been reported in about 1.3 percent of aborted equine fetuses from 1926 to 1947 in Kentucky.⁵ In a recent report from the same station the incidence had risen to 9.7 percent. The contracted foal syndrome was the most common anomaly at 3.8 percent.¹⁸ Further studies on the causes of these anomalies and their increased incidence is needed. Chromosomal

defects of the equine zygote as in other animals (See abortion in cattle) may cause early embryonic deaths. These defects are favored by aging of the spermatozoa or ovum prior to fertilization which is highly possible in mares due to their long estrous period. A review and study of the cytogenetic basis of prenatal loss in the mare while inconclusive indicated the need for further studies.³

Miscellaneous causes of abortion

Twinning is the cause of 20 to 30 percent of all observed equine abortions.^{16,18,20b} Double ovulations are reported in 4 to over 40 percent of estrous periods, especially in a few mares prone to twinning.^{2,8a,b,9,15} Double ovulations are most common in young and middle-aged mares and toward the end of the breeding season.⁹ Twinning is rare in ponies.⁸ Twinning in mares may be due to genetic factors. However, only 0.5 to 1.5 percent of mares give birth to twins.^{9,17b} The mortality rate of equine twins greatly exceeds that in any other domestic animal. Most equine twin zygotes undergo early embryonic deaths.^{8b,9} Certain mares, as cows, apparently produce twins more frequently than other mares;^{8b} one mare observed by the author aborted twins in 4 of 9 gestation periods. About 60 to 80 percent of twin fetuses that survive through the fourth month of gestation are aborted from 5 months to term with 72.6 percent from 8 months to term. Of 124 twin fetuses 31 were born alive and only 18 or 14.5 percent survived to 2 weeks of age.⁹ A failure of the placental vessels of the allantois chorion of one twin to anastomose with the other, possibly because of the early physical distance between the two blastocysts together with a lack of sufficient placental area for adequate nutrition of one of the fetuses results in the death of that fetus and the abortion of both fetuses.^{6,9} Occasionally the larger twin may die and be aborted with the living smaller fetus. Occasionally mummification or maceration of the dead fetus will occur with its subsequent expulsion at a later date when the other fetus is aborted or born at term. This unequal size of the placental areas available for nutritional exchange probably accounts for the unequal size of most equine twin fetuses by growth retardation of the "malnourished" twin.⁹ Mares cannot increase the size of the uterus or placenta to accommodate twins. The differences in the size of the twin chorions may be due to the time of fertilization or implantation of the zygotes or the rates of growth of the placentae. This is often incorrectly diagnosed as superfetation. Since it is probable that in the latter half of gestation in the mare progesterone necessary to maintain pregnancy is produced in the allantois chorion, it may be possible that abortion is due to a sudden drop in pro-

gesterone levels or a rise in prostaglandins or both caused by the death of one fetus and its membranes (See progesterone deficiency).

Since twinning is the second most common cause of abortion^{1,9,16} various procedures have been attempted to avoid or prevent twin pregnancies, especially in the occasional twin-prone mare. These include:

1. Rectal examinations at daily or more frequent intervals are performed, especially in the twin-prone mare and,

a) Breeding is only permitted when one mature follicle is present. Care must be used here because sometimes a follicle develops rapidly late in estrus and ovulates, asynchronous ovulation.

b) If two mature follicles are present then one may be tapped by an ovarian needle per vaginum.

c) Wait until one follicle ovulates and then breed 12 to 18 hours later since the life of an unfertilized ovum is only about 10 to 12 hours.

2. In the future ultrasonography may aid in diagnosing double follicles and early twin pregnancy, 15 to 30 days of gestation. This equipment presently is very expensive. (See Pregnancy Diagnosis, Chapter II.) By ultrasonography and rectal palpation twin pregnancy should be diagnosed if possible before 35 days of gestation. This may be difficult because the embryonic vesicles are small, may lie nearly together or one may be in the body of the uterus. If pregnancy is terminated after 38 days of gestation it is very difficult to get a mare to conceive that year because of the presence of the endometrial cups and the erratic estrous cycles, anovulatory estrous periods and the long time, usually 40 to 60 days or more before a normal ovulatory cycle occurs. If twin pregnancy is diagnosed then one can:

a) Douche the uterus, cause abortion and rebreed at the next estrous period which occurs normally within 10 days if the pregnancy is terminated before 35 days.

b) Inject the usual single luteolytic dose of prostaglandin or its analogue to abort the embryos before 35 days with estrus occurring as in a).

c) Destroy one embryo as early as possible, 20 to 35 days, usually by manual means. The other embryo often survives.^{7,11b,22} The administration of progesterone and an antiprostaglandin such as butozolidin or flunixin meglumine ("Banamine") before manually crushing one embryo might be indicated to prevent the loss of the remaining embryo. Further controlled trials are indicated. Ultrasonography for the early diagnosis of pregnancy, <30 days, makes such experiments possible. With the death of one embryo, both usually succumbed if surgical intervention or aspiration is employed.^{8b}

d) Allow the pregnancy to proceed. Most twin pregnancies are lost by the death of one or both embryos or fetuses as described under progesterone deficiency in this Chapter. The mare with twins may be put on supplemental injections of progesterone and watched closely. If signs of udder development or perineal and vulvar relaxation occur immediately give large doses of progesterone for 10 to 14 days. This may prevent the twin abortion. At term a normal, usually small, single foal is born along with a mummified, dead fetus.

None of these procedures used to prevent or "treat" equine twin pregnancies is highly satisfactory in the handling of this common condition except the manual crushing of one chorionic vesicle early in gestation or the administration of progesterone late in gestation to prevent abortion. Both of these practices require further controlled investigation.

Early embryonic deaths in horses have received little experimental study. Contagious equine metritis (CEM) due to *Hemophilus equigenitalis* is the only venereal disease causing early embryonic deaths in horses. Most recognized abortions in mares occur after 4 months of pregnancy. However, many unrecognized and unseen expulsions or abortions of embryos and fetuses probably occur from 8 days to 4 months of gestation. In the first few months of gestation maceration and partial or complete absorption of the dead conceptus may occur.^{17b,19} Probably most of these macerating embryos are expelled after a variable period except in cases involving the death of only one of twin embryos with the other embryo remaining viable.^{2,8b,14b,33b}

Many cases of early embryonic death, especially from 20 to 60 days of pregnancy, are erroneously diagnosed as failure of conception, "missed" or "silent" estrous periods, "spurious" conceptions or pseudopregnancy.⁸ A mare with a "spurious" conception has been serviced by a stallion, apparently conceived, and failed to exhibit estrus thereafter, even with a good "teasing" program. She exhibits normal vaginal signs of pregnancy but is not pregnant when examined rectally 30 to 50 days after service. This same condition of pseudopregnancy also occurs commonly in the bred or unbred mare due to a persistent corpus luteum.⁸

Recent studies based on embryo recovery in embryo transfer experiments show that about 80 percent of mares are pregnant at 8 days of gestation but at 35 days only about 65 percent are pregnant, a 15 to 20 percent loss of embryos.^{17c} On well-managed farms with veterinary supervision of the mares, a 2 to 10 percent and occasionally up to 20 percent loss of embryos and fetuses is experienced between routine pregnancy diagnoses at 40

and again at 110 days of gestation.^{3,4,10} An incidence of 21 percent early embryonic death loss the second month of pregnancy in 573 foaling mares compared to only 2 percent loss in barren mares was reported.¹² The incidence was highest in the mares conceiving on the foal estrus. The possible relationship between these early embryonic deaths and lactation was considered. Embryonic deaths from 25 to 31 days of gestation associated with malnutrition was reported.¹⁹ On the basis of studies in other species, some of these losses in mares may be presumed to be due to genetic or chromosomal defects resulting in improper development of the embryo or fetus.³ One infertile stallion produced conceptions with twice the early embryonic death loss of other stallions.⁴ Increased embryonic death loss may result from an abnormal uterine environment in mares infected with *Streptococcus zooepidemicus*, klebsiella, pseudomonas or other bacteria. Bacterial infections are often associated with improper closure of the genital tract due to poor conformation, lacerations and chronic scarring of the vulva resulting in pneumovagina, severe chronic lacerations or scarring of the cervix, and cystic degeneration of the endometrium in older mares. Some mares may lack sufficient progesterone to maintain early pregnancy as discussed previously.

Platt¹⁶ reported on factors influencing the incidence of abortion and noted that abortion rates, 21 percent, were higher in foaling mares conceiving from 7 to 21 days postpartum, compared to mares conceiving 22 to 42 days, 15.2 percent and over 42 days postpartum, 6.3 percent. The abortion rate of mares increased with increasing age, especially in mares over 18 years of age when it reached 28.6 percent. The incidence of abortion in brood mares barren for one year was 13.6 percent compared to 6.5 percent in mares that had foaled and conceived the same year. Abortion rates in mares covered by different stallions varied from 7.1 to 27.8 percent. Thus many factors can influence the incidence of abortion in mares. Further controlled, complete, competent studies on large numbers of infertile and fertile mares, as has been done in cattle, are indicated.

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(Nutritional, Genetic, Teratogenic, Physical, Twinning, Early Embryonic, Managerial)

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Abortion in Swine

Abortions in swine, as in other species, are comprised of early embryonic deaths and abortions or absorptions, fetal deaths and either abortion of the entire litter or mummification and stillbirths at term of a variable portion of the litter. The latter two categories in contrast to uniparous animals are common in swine. In a herd relatively free of infectious bacterial and viral diseases an incidence of 3 to 8 percent stillbirths and 1 to 5 percent

fetal mummification in 551 litters of over 5000 pigs in a ten year period was reported.² Abortions were uncommon. Over 58,000 pigs had an incidence of 5 to 14 percent stillbirths.⁵ Stillbirths comprise those fetal deaths occurring within the last 20 to 30 days of gestation which terminate in abortion at term; mummification comprise those deaths occurring from 35 to approximately 85 days of gestation.² The incidence of swine abortion is variable, possibly about 5 percent, and abortions usually occur from 75 to 95 days of gestation.^{2,10} Stillbirths and mummification will be discussed later in more detail but are an integral part of the porcine prenatal death loss.

About 40 to 50 percent of the causes of abortions in swine are diagnosed when investigated by competent veterinary laboratories. This level of diagnosis is only slightly better than in cattle and lower than in sheep and horses. A 1978 study of infectious agents associated with 824 abortions in swine in the midwest indicated that 38.8 percent of the fetuses revealed an infectious agent; 22 percent were viral and 16.5 percent were bacterial. Of the bacterial infections leptospiral agents were most common, 9.8 percent.⁴

Infectious Causes of Swine Abortion

Bacterial Causes

Leptospirosis first recognized in 1950 is the most common bacterial cause of swine abortion in the U.S. now that brucellosis is on the decline due to regulatory activities. The causative agent is usually *L. pomona* al-

Table 11. Summary of Causes of Abortion in Swine

Infectious causes:

Bacterial-Leptospirosis (*L. pomona*, *L. grippityphosa*, *L. icterohemorrhagiae* and *L. canicola*), Brucellosis (*Br. suis*) Miscellaneous bacterial-streptococci, *Staphylococcus aureus*, *E. coli*, *Salmonella* spp., *Mycobacterium avium*, *Listeria monocytogenes*, *C. pyogenes*, *Erysipelothrix rhusiopathiae*, *Pseudomonas* spp. *Nocardia asteroides*, *Pasteurella* spp, *Mycoplasma*, *Actinobacillus equuli*, *Actinomyces*, *Hemophilus*, *Proteus*, *Chlamydia*, *Hemophilus parahemolyticus* *Mycobacterium tuberculosis*, and *Klebsiella pneumoniae*.

Viral-enteroviruses or picornaviruses, parvovirus, pseudorabies (Aujeszky's disease)

Miscellaneous viral-hog cholera, reovirus, cytomegalovirus, vesicular exanthema virus and vesicular stomatitis virus, foot and mouth disease virus, Japanese B. encephalitis virus, hemagglutination virus, influenza virus and African swine fever virus.

Mycotic or fungal-*Aspergillus fumigatus* and other molds

Protozoa-*Toxoplasma gondii*, eperythrozoonosis, and sarcocystosis.

Noninfectious Causes:

Chemical, Drug and Plant-dicoumaral, zearalenone and trichothenes (moldy corn), pentachlorophenols (PCB's), carbon monoxide and creosote

Hormonal-estrogens, glucocorticoids, prostaglandins

Nutritional-deficiencies of iodine, vitamin A, iron, and calcium

Physical-stress and exhaustion coincident to transportation, fighting and injury

Genetic, congenital or chromosomal-anomalies, early embryonic deaths

Miscellaneous-poor management, increased stillbirths associated with large or small litters and in older anemic, fat sows.

though *L. grippotyphosa*, *L. hardjo*, *L. canicola*, *L. hyos*, *L. sejroe* (hebdomadis), *L. icterohemorrhagiae*, *L. ballum* and *L. autumnalis* have also been reported as causing abortion, stillbirths or weak pigs that die shortly after birth.^{1,2,3,4,6,7,1,2} Leptospirosis in swine due to various serotypes is widespread in the U.S., Europe and other countries throughout the world. It is more prevalent than commonly suspected because certain serotypes (serovars) produce an inapparent clinical disease.⁷ The incidence of leptospirosis in swine in the U.S. varies from 8 to 25 percent^{3b,5} with the higher incidence in Florida and Georgia.

Leptospiral organisms usually enter the body of the susceptible pig through breaks in the skin or through the mucous membrane of the nasal, conjunctival, digestive or reproductive tracts. A leptospiremia and general infection develops in which organisms invade all the visceral organs. This lasts for 5 to 10 days after which serum antibodies can be detected. The highest serum antibody titers are observed about 3 to 4 weeks after exposure and persist for a year or more. The organisms usually localize in the kidney tubules and are discharged in the urine for 1-1/2 to 6 months. In a few pigs the renal carrier state or leptospiruria may persist for 2 years. The greatest number of organisms are shed 20 to 30 days after exposure.^{1,5,7} Leptospiral organisms may be spread directly by the urine or indirectly by contaminated feed and water to susceptible pigs. As reported previously under abortions in cattle, leptospira can survive in a moist environment outside the body for a period of over a week.^{7,9} Infected boars might infect susceptible sows at coitus and have been shown to introduce the infection into a susceptible sow herd. It is possible that leptospirosis might be spread from infected boars by artificial insemination. Infection, but not abortion, was produced by infecting sows intravaginally after coitus.³ Abortions occurred only in sows infected late in the second month, during the third month or early in the fourth month of gestation. *Leptospira spp* can also be spread from cattle to swine or swine to cattle by infected urine. As in leptospirosis in cattle, wild animals such as rodents, skunks, opossums and raccoons may be a source of infection for swine.

Only occasionally do swine infected with *Leptospira spp* demonstrate acute or obvious clinical signs of illness such as hemoglobinuria. In experimental animals the incubation period is 1 to 2 weeks and inappetence, a mild fever and slight depression may be seen for several days during the leptospiremic stage of the disease but under farm conditions these signs are often not observed. Thus many leptospiral infections of swine are inapparent except for abortions that occur in pregnant females. Fol-

lowing leptospirosis in swine small widespread greyish foci are found scattered throughout the kidneys and liver.^{5,9} Some degeneration and necrosis of kidney tubules may also be present.

Abortions in susceptible sows infected with *Leptospira spp* occur 1 to 4 weeks prior to term. Of 800 aborting sows the earliest leptospiral abortions were from 72 to 78 days of gestation.⁴ Infections occurring between 55 and 88 days of gestation in sows most commonly produce abortions. Abortions usually occur 3 to 4 weeks after the initial infection of the sow. Some or all of the fetuses may be infected and deaths are due to a leptospiral septicemia. Following fetal deaths mummification of the fetus may occur.⁷ Stillbirths or deaths of fetuses late in gestation, and the birth of infected weak, "squealer" pigs that die within several days after birth are common in leptospiral epizootics in swine herds. The incidence of abortion in sows in a herd or of dead fetuses or dying newborn pigs may vary from 20 to 100 percent depending on the number of susceptible sows in late gestation and the rate of spread and virulence of the organism.⁸ Aborted fetuses may be icteric and weak live pigs may die soon after birth.^{6,7}

Leptospirosis may be diagnosed by leptospiral serum titers of 1:100 or higher in the aborting sows as determined by the microscopic agglutination (MA) test using cultures or antigens of five serotypes.⁷ Other serologic tests may be used. Low titers might indicate a prior infection or vaccination with *L. pomona* or other leptospira and abortion due to another cause. A rising titer is highly diagnostic in blood samples taken at abortion and several weeks later. *Leptospira spp* can often be isolated on culture with special media or animal inoculation from the liver, kidneys, peritoneal or pericardial cavities of aborted fetuses, stillborn or weak, ill newborn piglets. Histopathological examination of silver-stained kidney sections or fluorescent antibody stained body fluids or tissues^{6,7} from fetuses may reveal the organism. *Leptospira* often cannot be isolated from the urine of acutely infected aborting sows but several weeks following abortion leptospira can frequently be cultured from the sow's urine. Direct dark field examination of the fetal pericardial or peritoneal fluid or kidney scrapings may reveal the small, fine, filamentous, motile "spinning" leptospiral organisms.^{2,6,1} Following abortion caused by leptospira the sows are immune and resistant to reinfection with that serotype for at least 11 to 14 months.⁶

Leptospirosis in swine may be controlled by sanitation, vaccination and antibiotic therapy, but is difficult to eradicate in a herd. Maintaining a herd free of leptospirosis is possible but may be difficult due to reservoirs of infection in cattle, other domestic animals and

in wild animals, such as skunks, mice and rats. A sanitary environment free of water holes and swampy areas may aid in preventing the spread of the disease. Covered feeding and watering troughs not easily contaminated by infective urine are also desirable. Cattle and swine should not be housed together as leptospirosis may be transmitted between the species. By proper sanitation and management, frequent blood testing, segregation and isolation or measures used to produce a specific pathogen-free herd, a leptospirosis-free herd may be attained. If the swine herd is free of leptospirosis, purchased swine should be negative to the blood test, isolated away from the herd for a month and retested before placed in the herd.

Since in chronically-infected swine herds the acute disease is inapparent, most commercial swine owners routinely vaccinate their sows and gilts before the breeding season, early in pregnancy or every six months with a multivalent leptospiral bacterin that provides a good but relatively short-lived immunity against abortions due to *L. pomona*, *hardjo*, *grippotyphosa*, *canicola* and *icterohemorrhagiae*. The bacterin may also be used early in an outbreak but abortions may continue for 3 to 4 weeks in infected sows. Vaccination of swine two weeks before going to fairs or shows is recommended. Leptospirosis may occasionally develop in exposed vaccinated sows but abortions do not occur, and the number of carriers will be reduced.^{5,1} Vaccination with the bacterin produces low serum titers.

In recently infected susceptible herds, vaccination and antibiotics administered for a period of several weeks⁶ have been effective in treating the carrier state as well as the acute infection and to reduce the incidence of abortion for a period of several weeks until immunity develops to vaccination. The following regimens have been recommended: for pregnant animals in an infected herd; 400 to 500 gm. of chlortetracycline (*Aureomycin*) or oxytetracycline (*Terramycin*) per ton of feed for 10 to 14 days should be provided. For treating the chronic carrier or shedder state in pigs of all ages, chlortetracycline or oxytetracycline at levels of 400 to 500 up to 1000 gm. per ton of feed should be fed for 7 to 10 days.^{2,6,1} Individual treatment of swine may also be used with 5 daily intramuscular injections of tetracycline (*Polyotic*) at a dose level of 3 mg. per pound of body weight or a single injection of 25 mg. per kg. of body weight of dihydrostreptomycin.¹⁰

It is advisable to blood test boars or sows introduced into the breeding herd. If the breeding herd is infected, vaccination of these animals prior to entry is indicated. If the breeding herd is noninfected and the introduced animals are positive, isolation and administration of antibiotics to eliminate the carrier state is essential.

Brucellosis in swine, due to *Brucella suis*, is a much more insidious disease than brucellosis in cattle. The disease has been widespread especially in the hog-raising areas of the Midwest. In 1980 the incidence of animal infection in the U.S. was 0.08 percent and farm infection 0.87 percent.⁵ An aggressive eradication program is continuing in the U.S. under the direction of the U.S. Dept. of Agriculture and cooperating states to increase the numbers of validated (brucellosis-free) herds. Blood testing of adult sows and boars at slaughter to locate infected herds has proven highly effective in controlling and eradicating this disease. Swine brucellosis exists in all swine producing countries and occurs in wild pigs in Florida and Louisiana.⁷ In Florida infected feral swine have caused brucellosis in other swine and hunters.⁶ *Br. suis* may also occur naturally in horses, cattle, dogs, fowl and the European hare. *Br. abortus*, *Br. melitensis* and *Br. canis* may cause brucellosis in swine but clinical signs are rare and the infections are self-limiting.^{2,5,6} Brucellosis due to *Br. suis* until recently was the most common type found in humans in the United States.⁶ *Br. suis* is a facultative intracellular parasite that can survive in the host's phagocytic cells.³

Clinically the disease is endemic on certain farms. The level of resistance is high in young immature pigs nursing infected dams. Clinical signs of the disease usually occur after sexual maturity.^{2,6,4} New infections in a herd are often traced to a recently introduced boar. The organism, *Br. suis*, enters the body through the conjunctiva, nose or mouth, the latter by ingestion of feed and water contaminated by uterine discharges, urine, or feces of infected animals or by eating aborted fetuses and membranes. An important cause of infection in the sow is mating with an infected boar. Brucellosis is a venereal disease of swine. Most infected swine develop brucellosis with clinical signs and a bacteremia starting 1 to 7 weeks post exposure and continuing for 5 weeks and then in a few swine an intermittent bacteremia may last for 8 months to 3 years.⁶ A diagnostic level of serum antibody develops 10 to 21 days after exposure. Antibody levels are higher and persist longer in adult than in immature swine.

The principal clinical signs of brucellosis in swine are abortion, birth of stillborn or weak pigs, infertility due to early embryonic deaths, and less commonly orchitis in boars and posterior paralysis and lameness due to vertebral lesions. Abortions may occur at any stage of gestation.^{6,2} Nearly all brucella-infected boars had lesions in the epididymis and vesicular glands and produced normal appearing but infected semen.⁶ Pus in the semen was uncommon and fertilization was normal. Following service to infected boars abortions may occur as early as

22 days of gestation and are usually not observed under field conditions as no vaginal discharge is present. Sows or gilts infected at coitus frequently return to estrum in 30 to 45 days. Infections acquired by the sow after 30 or 40 days of gestation result in abortions from 46 to 105 days, average 65 to 80 days.^{2,6,4} Genital infection may persist from 1 to 30 months in females. The period of infertility in sows is related to the duration of the genital infection and the degree of pathology present. Many sows overcome the genital infection within one to two months and then have good conception rates thereafter. **Br. suis** may persist in granulomatous lesions and in mucosal cysts of the endometrium and catarrhal endometritis may occur. About 75 percent of susceptible gilts bred to an infected boar become pregnant and 80 percent of these have a normal gestation period. But when an infected sow was bred to a clean boar only a 35 percent conception occurred due to chronic endometrial lesions causing early embryonic deaths and prolonged periods between estrums.⁶ Nodular or granulomatous lesions containing **Br. suis** may also be found in lymph glands, spleen, liver, kidneys, testes, ovaries, and accessory male reproductive glands.

A good herd history is very helpful in a diagnosis of swine brucellosis. The disease may be definitely diagnosed by recovering the organism by cultural methods from organs, especially lymph glands, of the infected sow or boar, from the stomach contents of aborted fetuses or from the chorion of the placenta. Fluorescent antibody tests on fetal or placental tissues may aid diagnosis. The tube or plate agglutination tests may be performed on blood serum from suspected or infected swine. This test is not as reliable as the blood test in cattle. Certain swine harboring and spreading the organism may have low serum titers or be negative to the agglutination test. Most swine with localized infections and those with clinical signs of brucellosis will have an agglutination titer of 1:100 or higher on the standard tube test at some stage of the disease.^{6,4} Nonspecific antibodies to other organisms producing titers of up to 1:50 are common in swine. The blood titer in swine drops more rapidly than in cattle. Testing the herd and eliminating the reactors is not a practical method of eradicating the disease. The agglutination test is of value, however, as a herd test for indicating the presence of infection. In the adult swine herd the presence of any reactors with a titer of 1:100 or a higher indicates that the herd is infected.³ A herd with no animals with titers over 1:50 on repeated tests and no clinical signs of brucellosis is considered negative. Supplemental tests such as the acidified plate antigen test, the heat inactivation test, the Rose-Bengal test, the rivanol test, the complement fixation test and espe-

cially the Card test may be helpful in the diagnosis of carriers of **Br. suis**.^{3,6,7} In the future the ELISA (enzyme-linked immunosorbent assay) test may prove to be a superior test.⁶ A single negative blood test on one individual is of no diagnostic value. The prognosis is guarded in this insidious disease, since sterility may follow abortion and the sow may spread the disease for several months or more. In respect to the herd situation, rather drastic steps need to be taken to eradicate the disease, as there are no treatments that have proven effective in curing an infected animal or herd. No safe or reliable vaccines have been developed and in this country the present incidence of brucellosis does not justify a possible vaccination approach to control.

The methods of eradicating the disease in commercial herds consist of^{6,3} (1) selling all the stock for slaughter, cleaning and disinfecting the premises or moving to clean quarters and then restocking from known noninfected or validated herds. This has been the most successful and economical approach. (2) In valuable purebred herds in which it is desired that breeding lines be maintained, the pigs may be raised on infected sows until eight weeks of age, weaned, and moved from the infected herd, isolated, and raised on clean ground. These pigs are tested individually by the agglutination test at intervals of 1 to 2 months. Any reactors are sold for slaughter. Methods of blood collection from the anterior vena cava and the tail of swine have been described.^{2,3} When the isolated gilts are of breeding age they are bred to noninfected boars. After farrowing in isolation the gilts are retested and if they are negative their litters, when weaned at 8 weeks, are the basis of a new, clean herd. The original herd is disposed of as soon as practical. (3) Repeated blood testing at 30-day intervals together with the slaughter of reactors may occasionally be advisable and successful. In most herds this is not as satisfactory or successful as the two previous methods. If only one or two animals in a herd are serologically positive there is a question whether brucellosis actually is present in the herd.^{6,3} Chemotherapy is of no value in this disease. **Br. abortus** strain 19 vaccine does not immunize swine. Natural resistance or immunity to **Br. suis** is present in about 30 percent of swine.^{6,4} Animals purchased from herds of unknown brucellosis status should not be placed in a brucellosis-free herd.

Miscellaneous bacterial causes of abortion in swine have been described in sporadic cases or occasional outbreaks. The following organisms have been recovered in pure culture from freshly-aborted porcine fetuses: **Staphylococcus aureus**,⁹ **Mycobacterium avium**,⁶ **Listeria monocytogenes**,⁷ **Salmonella sp.**, **E. coli**, **Streptococci**,^{9b} **Coryn. pyogenes**,^{4,5} **Erysipelothrix rhu-**

siopathiae; *Pseudomonas* spp., *Pasteurella*,^{2, 1a} *Campylobacter fetus*, mycoplasma,^{16c} *Nocardia asteroides*,⁴ *Actinomyces* spp.,^{4, 5} *Actinobacillus equuli*,¹¹ *Haemophilus parahemolyticus*, *Mycobacterium tuberculosis*, chlamydia and *Proteus*.^{4, 8}

An outbreak of abortions, stillbirths and moribund neonatal pigs apparently due to streptococci and *E. coli* has been described.^{1a} The former organism was resistant to 4 antibiotics that had been used in the herd in prior years as a feed additive. The use of effective oral antibiotics, determined by sensitivity testing, for the last 30 days of gestation greatly increased the numbers of live pigs per litter at birth, 10 vs. 6, and the number of weaned pigs per litter over the untreated controls, 8.5 vs. 3.8, respectively. *E. coli* endotoxin caused abortion when injected into pregnant sows by apparently inducing prostaglandin release and luteolysis.¹² Nine of 30 sows given a live avirulent erysipelas vaccine 30 days before farrowing aborted and the organism was isolated from the fetuses.³

Viral Causes for Porcine Prenatal Losses

The major viral causes for prenatal loss in swine are parvovirus infection, pseudorabies or Aujeszky's disease and various entero-picorna (SMEDI) viruses. Hog cholera, formerly an important viral cause of abortion, has been eradicated from the United States. SMEDI is an acronym coined by Dunne³ referring to stillbirth-mummification-embryonic death and infertility associated with the above and other viral diseases of swine. Other viral agents of swine that produce signs of the SMEDI syndrome are hog cholera virus, reovirus and influenza virus.^{1, 2, 3} Of 824 porcine abortions in the midwest U.S.A. 22 percent were due to a viral agent; 10.9 percent enterovirus, 4.9 percent parvovirus, 4.4 percent reovirus and 1 percent pseudorabies virus.⁴ Dual infections with two viruses or a virus and bacteria are fairly common in swine abortions. Since the etiologic agents causing the SMEDI syndrome are now well-known and diagnostic tests have been developed, the term SMEDI should be discarded. It should be noted that leptospirosis and brucellosis may also exhibit similar signs. It is important to recognize that in swine these and other viruses may affect the developing embryos or fetuses and result in: (1) infertility or sterility related to early embryonic deaths that are aborted unseen or absorbed, (2) fetal mummification, (3) defective or anomalous fetuses (4) stillbirths (5) birth of live but poorly viable pigs and (6) birth of live normal pigs that may be carriers of the virus. Abortions of entire litters late in gestation are rare.

Enteroviruses or Picornaviruses,³ have been shown to cause occasional abortions but mainly the aforementioned effects on intrauterine embryos or fetuses in sows. (See Figure 74.) These enteroviruses are ubiquitous in all swine. The only known natural host for porcine enteroviruses is the pig. These viruses are quite resistant to disinfectants and very resistant to environmental influences.² Transmission is directly by the fecal-oral route and indirectly by fomites. Several serogroups of porcine enteroviruses are endemic in all commercial swine herds. Pigs of any age are susceptible but most adults have high antibody titers and rarely excrete virus.^{2, 4} In a tentative classification of over 40 porcine picornavirus strains isolated in North America, Japan, England and Czechoslovakia, 17 groups were determined serologically. The 5 strains of enteroviruses isolated in Pennsylvania fell into Groups 1, 6, 7 and 13.⁵ These 5 strains of enteroviruses when inoculated into cholera-immune or cholera-susceptible pregnant swine cause a similar syndrome to that caused by hog cholera, pseudorabies, parvovirus, or other viruses that will be mentioned. Susceptible pregnant gilts inoculated with enteroviruses at 25 days of gestation had embryonic deaths within 5 days of the inoculation; death of fetuses and mummification occurred 15 to 40 or more days after inoculation; and thereafter stillbirths and weak pigs dying within 6 hours after birth were observed. Fetuses in the same sow may become infected and die at different stages of gestation. If embryos die before 30 days of gestation when no skeletal development has occurred, absorption results; if fetuses die at later stages of gestation, 50 to 100 days, after skeletal development occurs mummification or stillbirths result. The position of the fetus in the uterus was not related to the time of fetal deaths. In some sows where early embryonic deaths occurred the sow returned to estrum at a varying interval following the initial service. In other cases where fetal deaths occurred at 30 to 60 days of gestation and mummification resulted, "parturition" did not take place at the end of gestation and the sow exhibited a prolonged "gestation" period. These signs are usually limited to one breeding season in a herd. Recovered immune sows have normal gestations during the next breeding season.

The virus is apparently spread through the susceptible animals in the breeding herd after its introduction by an infected animal or from contact with infected pigs. The boar may also be a temporary spreader of the virus. The virus may be isolated in suspected outbreaks from cultures of the internal organs of stillborn fetuses or weak, poorly viable, newborn pigs. Usually there are no lesions in aborted fetuses. Occasional lesions may be seen in the CNS, lungs (pneumonia) or heart (pericarditis or myocarditis). In mummified pigs the viral antigen may

be detected by immunofluorescence. Serologic tests are of no value.² Sows infected before breeding are apparently immune as are sows at the next breeding period following an episode or outbreak of stillbirths, mummified fetuses, abortions, embryonic deaths and infertility. Control measures depend on prevention rather than treatment.² Because of the many serogroups no effective vaccine is available. So gilts and fresh stock introduced into the herd should be exposed to "resident" infection by contact with the older sows, weaned piglets, or fecal material a month or more before breeding. Comingling gilts with older sows also provides nose to nose contact as well as fecal exposure and the development of a natural immunity before breeding.^{1,2}

Pseudorabies (Aujeszky's disease) due to a herpesvirus is widespread in swine in the U.S. with most outbreaks reported in the midwest. In the early and mid 1970's there was a marked increase in the number and severity of outbreaks in the U.S. In 1981 the incidence in swine based on serological testing by the USDA was 8.3 percent. The disease incidence has also increased in Europe and is found world-wide.^{3,1b,5,13} The virus apparently persists in a latent form^{3,3,5,7,11} in recovered swine and may be present in most domestic animals and many wild animals. In animals other than swine, which is the host of the virus, pseudorabies is usually a fatal disease. Humans are resistant. Up to 60 percent abortions have been reported in a susceptible breeding herd.^{5,8,12} The average live litter size was reduced from 7.7 pigs in control gilts to 1.9 pigs in the exposed gilts.⁸ Forty-one percent of porcine fetuses from sows aborting or delivering stillbirths due to pseudorabies had pinpoint to poppy-seed-sized necrotic foci in the liver and intranuclear inclusion bodies were observed.^{2,14} They also have isolated the virus from the vagina of sows and the prepuce of boars. If this herpesvirus is like others in domestic animals it is likely the boar may transmit the virus at coitus at rare intervals.⁹ The herpesvirus of pseudorabies in swine, as in virus infections in other species, such as IBR in cattle, may be transmitted in semen. Many states and the federal government have passed regulations in recent years controlling the shipping of infected swine or semen, the use of vaccines and the quarantining of known-infected herds.

The greatest mortality in susceptible pigs infected with pseudorabies virus from nasal or oral exposure is in suckling pigs, up to 90 percent, and next greatest is in weanling and fattening pigs.^{4,5} Usually fever, difficult breathing and sneezing, salivation, vomition, anorexia, ataxia, convulsions, coma and death in 1 to 2 days in the former and 6 to 8 days in the latter is observed. The mortality rate in mature swine is less than 2 percent with

mild signs of sneezing, coughing, anorexia. Blindness often is associated with central nervous signs. Most older pigs recover in 10 to 12 days.⁵ The main site of viral replication is the upper respiratory tract from which the virus invades the blood stream and the cranial nerves.^{5,7} Viremia allows passage of the virus to all organs of the body.

In pregnant swine the virus readily crosses the placenta barrier and infects the embryo or fetus. If this occurs at 30 days of gestation the embryos die and are resorbed and pregnancy is terminated. If infection occurs after 40 days of gestation and before 60 to 80 days, fetal mummification and maceration of some or all of the fetuses may occur. If infection occurs after 60 or 80 days of gestation death and maceration, premature expulsion or the birth at term of stillborn or weak infected fetuses may occur. Delayed parturition of 2 to 3 weeks occasionally occurs if all the fetuses died in the later stages of gestation. Following fetal infections and expulsion, infertility may be present at the first breeding.

Diagnosis of pseudorabies can be made by culturing tissues from infected fetuses or performing the immunofluorescent antibody (FA) test on fetal tissues.^{5,14} Serologic tests on live pigs or sows include the virus neutralization test, the enzyme-linked immunosorbent assay (ELISA) test, agar gel immunodiffusion test,^{7b} the complement fixation test and the indirect hemagglutination test. A skin test based on cell-mediated immunity has been developed. Biologic tests of animal inoculation of suspect material subcutaneously into rabbits or mice or into embryonating chicken eggs can also be performed.⁵

Treatment cannot greatly alter the course of the disease once signs of the disease are present. Eradication or control are topics being seriously debated currently between those concerned with the control and prevention of pseudorabies.^{13a} Because of the nature of herpesviruses and their ability to remain latent in the ganglions of the cranial (trigeminal) nerve^{7,11} and recrudescence under stress,^{1b} the wide-spread incidence of the virus in the swine population, the failure of diagnostic tests to indicate all carrier or infected animals, and the difficulties of acquiring a pseudorabies virus-free herd and maintaining it with the other livestock or wild animals that can carry the virus on to the farm, the author believes a pseudorabies virus-free commercial or conventional swine herd would be difficult to develop and maintain. The cost of this effort would probably not be economically possible for most swine breeders and the country.^{13a}

Attenuated (MLV) and inactivated vaccines are available^{1,5,6,10} and when used properly before breeding in young pigs will produce a good immunity and largely

prevent losses due to pseudorabies. Vaccines will not prevent infection with virulent virus and these infected animals shed the virulent virus for a period of time and often develop a latent infection that can recrudesce under stress.^{3,7,11} One bivalent commercial inactivated vaccine contains both pseudorabies and parvoviruses.¹⁰ Vaccines will produce positive serologic titers.⁶ These titers can interfere with serologic tests used to eliminate virus from a herd. Another inactivated P.R. vaccine has been combined with a multivalent leptospiral vaccine. It is recommended that cattle, sheep and dogs be kept away from infected or pseudorabies-free herds. Additions to herds should be blood tested and retested after a 4-week isolation period or purchased from pseudorabies-free herds to prevent the possible introduction of virulent virus especially when sows are pregnant or have recently farrowed. Pseudorabies vaccines have proven helpful when given to pregnant sows early in an outbreak.^{1,10}

Porcine Parvovirus (PPV), the most common cause of embryonic and early fetal loss or mummification, was first described in 1967 in England.^{1,5} Since then it has been found to be an ubiquitous virus throughout the world and is enzootic in most swine herds.⁵ It causes reproductive failure in sows with signs of embryonic and fetal death with resorption or mummification without producing any clinical signs of illness. In 1977 a study at an abattoir in Iowa found 62 of 203 pregnant sow uteri containing dead or mummified embryos or fetuses.³ Forty six or 74.2 percent of these litters were positive for porcine parvovirus (PPV) based on isolation of the virus or demonstration of the PPV antigen. Most of the fetuses (392 or 84 percent) died and became mummified before 71 days of gestation and antibody was found in nearly all of the serums of the 68 or 14.8 percent live fetuses at 81 to 105 days of gestational age. The incidence of PPV infection in pregnant uteri in abattoir material in Minnesota and Iowa was 9.4 to 23 percent.^{3,9} Porcine parvovirus is not related to other parvoviruses including canine parvoviruses, feline panleukopenia virus or mink enteritis virus.⁵

Because of the ubiquitous nature of porcine parvovirus nearly all sows in most herds have become naturally infected by the oral and nasal routes and are immune as determined by seroepidemiologic data. This immunity persists for a lifetime. The parvovirus is quite stable, and remains infectious in the secretions and excretions of acutely infected pigs for months.⁵ It is resistant to common disinfectants. Parvovirus may be spread by acutely-infected boars by several routes including the semen. Acute infection of susceptible young pigs, pregnant gilts or sows and boars is usually subclinical even though the virus is found throughout the body and can pass transplacentally to the fetuses. Thus the only clinical signs

are referable to reproductive failure with embryonic and fetal death.

Transplacental infection apparently requires 10 to 14 days from maternal exposure. Infection of the conceptus between 10 and 30 days of gestation causes embryonic death and resorption and between 30 and 70 days causes fetal death and mummification. Intrauterine spread of the virus may also occur causing deaths at different times with mummified fetuses of different sizes.^{4,5} Immuno-tolerance to PPV may develop in fetuses infected prior to 55 days of gestation and they may be born alive with no antibody but carrying the virus.⁵ After midgestation, 70 days, fetal infection also occurs in acutely infected susceptible gilts or sows but the fetus survives without clinical disease because it develops an immunologic response to the virus.^{5,6}

Even though a direct causal role of porcine parvovirus in semen in reproduction failure has not been completely confirmed, the susceptible female infected by semen may spread the virus to other swine.⁵ Conceptuses are apparently infected transplacentally during or after maternal viremia. Infected embryos or fetuses contain the virus in most of their cells at death especially in the endothelium as determined by immunofluorescent microscopy. Macroscopic lesions seen in fetuses before they are immunocompetent include congestion, edema, hemorrhage, and bloody fluids in the body cavities. Microscopic lesions include cellular necrosis and inflammation and possibly intranuclear inclusions.⁵ Meningoencephalitis with perivascular cuffing has been described in fetuses or stillborn pigs after they have become immunocompetent.

PPV may be suspected when gilts, not sows, show evidence of early embryonic deaths, return to estrus, have abortions, fetal mummification, resorptions, infertility and failure to farrow. Stillbirths or reduced numbers of pigs and neonatal deaths occur occasionally.⁵ Fetal mummification or death of all embryos and their resorption has caused prolonged gestation. Diagnosis is confirmed by fluorescent antibody test of tissues, especially the lungs, of mummified fetuses less than 16 cm in length.⁵ Remnants of autolyzed tissues of embryos may be similarly examined by immunofluorescent microscopy. Viral isolation from infected autolyzed tissues of fetuses is difficult. Serologic tests are recommended only when small mummified fetuses are not present indicating a recent infection. Maternal blood samples taken from sows or gilts if negative for PPV antibody would exclude this virus as a cause of reproductive failure. Because PPV virus is so ubiquitous a positive hemagglutination inhibition (HI) test, serum neutralization (SN) test, immunodiffusion test, or modified direct complement fixation (CF) test is meaningless.⁵ Detection of PPV antibodies

in the serum of fetuses or stillborn pigs or neonatal pigs before nursing or body fluids of fetuses would indicate fetal infection since maternal antibody cannot cross the fetal-maternal junction.²

There is no treatment for porcine parvoviral reproductive failures. Preventive measures include either the natural exposure and infection or vaccination of gilts before they are bred. Natural exposure and infection is effected by close contact or intermingling of seronegative gilts with seropositive sows, placing the former in a contaminated area or exposing the susceptible gilts to mummified conceptuses, stillbirths and placentas of recently infected aborting sows. This method of exposing gilts to PPV may inadvertently expose them to pseudorabies virus and other diseases and is not as reliable as vaccination. In herds where PPV is enzootic usually 50 percent or more of the gilts are infected and immune before breeding.⁵ In 2 swine herds with enzootic PPV, the proportion of seronegative, susceptible gilts at breeding was 40 percent and only 50 percent of these became infected during their first gestation. The incidence of mummified fetuses in pigs born previously to seropositive gilts, seronegative gilts and gilts that seroconverted during gestation was 0.6%, 1.0% and 3.0% respectively.^{2b}

By vaccination one month or more prior to breeding the swine breeder can be certain gilts are immune before conception. Both inactivated and MLV vaccines^{5,7,8} have been developed. Since seropositive sows produce antibodies to PPV in the colostrum passive antibodies in piglets persist for 4 to 6 months and interfere with vaccination immunity. Gilts should be vaccinated 15 to 60 days before breeding. The duration of immunity from the inactivated vaccine lasts 4 to 6 months and usually within this time natural exposure and active immunity will develop. Vaccination with an inactivated product is recommended for all seronegative sows and boars introduced into an infected herd. A few disease-free or other swine herds may be PPV-free but maintaining this status is very difficult and risky. Porcine parvovirus when introduced into a PPV-free herd produces very severe reproductive losses.⁵

Swine influenza due to the swine influenza virus (SIV) is primarily a respiratory disease common during the fall and winter in swine raising areas with a serologic incidence of 12 to 45 percent.^{7,5} Reproductive losses, including mummification and weak pigs, have been reported in susceptible dams infected with SIV during gestation, especially the first 30 days. Breeding sows that are more likely to have been previously exposed to SIV, in the fall for winter farrowing instead of gilts may reduce the reproductive losses.^{2,5,11} Diagnosis of swine influenza is based on the history and respiratory signs, and possibly the recovery of the virus from aborted fetuses

or careful interpretation of serologic evidence by the hemagglutination-inhibition (HI) or serum neutralizing or complement fixation test on sows or newborn piglets before suckling. Presently there are no licensed vaccines for swine influenza nor any specific treatment.¹ A recent study showed that SIV did not produce abortions, did not cross the placenta into the fetuses and was not a direct cause of reproductive failure in swine.^{1b} It should be noted that influenza viruses in cattle and horses seldom affect the fetus or reproduction. Further studies are needed to determine the role, if any, of swine influenza in reproductive losses.

Reovirus infection has been reported in 4.4 percent of 320 porcine abortions based on untyped virologic cultures.^{4,8} Sows experimentally infected between 40 and 80 days of gestation produced stillbirths, mummified fetuses and weak pigs.⁷ Clinical signs of reovirus infection in swine usually includes mild respiratory or digestive signs. No lesions have been described in fetuses or neonates. Antibody detected by the HI test is widespread but might be used for detecting antibodies in stillbirths or neonatal piglets before suckling. Reproductive losses due to reovirus requires further investigation.

Porcine cytomegalovirus (PCMV) infection is not accompanied by clinical signs in pigs over 3 weeks old but can be fatal for the fetus and newborn piglet.⁶ This ubiquitous organism is spread in the nasal and ocular secretions, urine and cervical secretions of infected pregnant sows. Active immunity usually develops between 8 to 11 weeks in piglets receiving passive colostrum immunity from the dam. Early postnatal or congenital infection of piglets occurs in association with mummified fetuses, stillbirths, neonatal deaths, and stunted pigs. Intracellular inclusions are observed in the reticuloendothelial tissues and kidney of infected fetuses or neonates. Gross fetal lesions include petechiae, pleural and pericardial effusions and edema especially in the kidney. Viral cultures and serologic tests aid the diagnosis of PCMV infections.

Hog cholera due to hog cholera virus (HCV), although eradicated from the United States, is present in many countries. Hog cholera virus strains differ markedly in virulence.¹⁰ Field strains of low virulence or attenuated or modified strains used as vaccines if inoculated into pregnant susceptible sows the first 10 to 20 days of gestation resulted in death and absorption of the embryos and fetal malformations.^{2,3} If the virus gained entrance to the sow's body from 30 to 90 or more days of gestation, mummification of fetuses, stillbirths and weak pigs were common.

The hog cholera virus in infected fetuses, stillbirths or live newborn pigs may be cultured on tissue culture media or demonstrated by the fluorescent antibody

technique^{1,2,4,10} Pigs infected **in utero** may survive and after birth become tolerant carriers of HCV. Under stress these carrier pigs may become ill and die of cholera weeks or months after birth.

Other viral causes for porcine fetal deaths, mummification and abortion include: **Japanese B encephalitis virus**, **Japanese hemagglutinating virus**, and **African swine fever virus**.^{1,4,9} The latter virus caused outbreaks in the Dominican Republic and Haiti in 1978 and Cuba in 1979. This has been the closest African swine fever outbreaks have occurred to the United States. This virus causes porcine abortions at any stage of gestation, latent carriers and possibly immunotolerant offspring. The Dominican isolate caused 7 abortions in thirteen 38 to 92 day pregnant sows 5 to 8 days postinoculation associated with the acute viremia of the sow.⁹ African swine fever virus was recovered from the aborted fetuses. Abortions have also been described accompanying acute cases of **vesicular exanthema**,⁷ foot and mouth disease and possibly **vesicular stomatitis**.^{7,4}

Mycotic or fungal porcine abortions due to **Aspergillus fumigatus**, **Nocardia asteroides** and others have been described on rare sporadic occasions.^{4,1a,b,c}

The parasitic protozoan causes of abortion in swine possibly include the agents of **Toxoplasma gondii** and **Eperythrozoon suis** and **Sarcocystis spp.** From serological evidence **toxoplasmosis** is common in swine but few clinical cases have been reported.^{1,3} Pregnant sows may abort or farrow weak or stillborn pigs.^{2,6,7} **Eperythrozoonosis**, although very common in herds in the United States, is suspected, but not proven to be associated with reproductive problems including delayed estrus, embryonic death, absorption of fetuses and abortion.^{6,5} **Sarcocystis suicanis** was carried by host dogs and raccoons and affected 16.6 percent of sows in Georgia. This parasitic protozoa caused abortions and deaths in pregnant sows in Europe,^{1a,4} when experimentally inoculated in large doses. (See sheep.)

Noninfectious Causes of Porcine Abortion

Chemical, drug or plant poisonings are rather seldom causes for abortion in swine. Dicoumarol poisoning has been cited.⁵ Wood preservatives such as the **pentachlorophenols** and **creosote** have been reported to be toxic for prenatal and postnatal pigs.¹⁴ Wood so treated should be thoroughly dried before placing sows or pigs in contact with it. Polychlorinated biphenyl (PCB) when fed to sows caused a reduction in live pigs farrowed and an increase in fetal mummification probably related to the immunosuppressive effects of the compound.⁶ **Moldy**

corn toxicosis probably due to aflatoxin B associated with penicillin, aspergillus and rhizopus molds, caused bloody diarrhea, anorexia, depression, ataxia and abortion.³ Another mold, **Fusarium spp.**, produces the mycotoxins, zearalenone and trichothenes.^{7a,b,9b,11} The former causes an estrogenic syndrome of swollen external genitalia, mammary gland development, testicular hypoplasia, infertility, constant estrus, pseudopregnancy, small litter size due to early embryonic deaths and resorption, increased mummification and possibly increased stillbirths and weak pigs. The latter mycotoxin may also cause infertility and abortion. **Ergot** was not shown to be a cause of abortion in swine even when ergotism produced necrosis of the extremities.¹ Ergot-infected feed did cause agalactia in sows and in one report lowered reproductive rates.^{3,7,9b,11} Early embryonic deaths and mummification followed the consumption by sows of a tropical shrub legume, **Leucaena leucocephala**.¹⁶

Hormonal causes for porcine abortions are uncommon. Glucocorticoids have not been reported to cause abortion in swine but severe stress conditions have been associated with premature births and abortions. Exogenous glucocorticoids in large doses such as dexamethasone and prostaglandins or their analogues have been used to induce premature or "timed" parturition by injection between 110 and 113 days of gestation.⁵ (See Chapter XI). Administration of 500 µg cloprostenol to gilts between 30 and 100 days of gestation resulted in abortion in 34 to 42 hours requiring a duration of 4 to 14 hours. Estrus occurred 9 to 10 days after abortions with 90 percent conceptions in this estrus.^{11b}

Nutritional causes of swine abortion, stillbirths and anomalous fetuses include deficiencies of iodine, vitamin A, iron and calcium.^{5,9,10,12} **Iodine deficiency** is characterized by hairlessness, goiter, edema of the fetus and a slightly prolonged gestation. This condition is rare at present because iodine is commonly added to salt in most rations. **Vitamin A deficiency** usually related to a lack of pasture, alfalfa hay and the feeding of 2 or more-year-old corn may result in weak, moribund newborn pigs or stillbirths with edema, ascites, cleft palate, anophthalmia, microphthalmia, hydrocephalus and cardiac defects. **Iron deficiency** may cause stillbirths or weak newborn pigs suffering from a severe anemia. **Chronic calcium deficiency** due to exclusive grain feeding, a lack of roughage or pasture or no mineral or tankage supplementation results a progressive increase in the number of mummified fetuses and stillbirths with each litter produced.

Physical causes of porcine abortion include stress and exhaustion due to transportation and excessive fight-

ing between sows.⁵ Abortions were associated with severe outbreaks of pneumonia in many swine herds.^{9a}

Genetic or chromosomal causes for stillbirths or moribund pigs include the congenital or genetic lethal defects described previously (See Chap. III). About 10 to 12 percent of the blastocysts from normal sows had chromosomal defects, mainly polyploidy, which may account for about 30 percent of the total pregnancy wastage in swine.⁸ These defective zygotes that die early in gestation may comprise a significant number of the ova released and fertilized that fail to result in pigs produced at parturition. This loss may be estimated by counting the corpora lutea in the ovaries at farrowing.

Miscellaneous abortions or loss of neonatal pigs may be due to **poor management** at the time of farrowing resulting in smothering, crushing or chilling of newborn pigs. These are often called "stillbirths." About 5 to 10 percent of all porcine fetuses expelled at parturition are stillbirths. These may be divided into prepartum deaths usually due to infectious causes late in gestation and intrapartum deaths associated with delayed or abnormal expulsion of fetuses.⁶ Attendance of a caretaker at farrowing is highly desirable. At parturition sows should be neither too fat nor too thin. Farrowing crates or guarded stalls and heat lamps or heated floors are very helpful in preventing neonatal losses. The larger the litter or the smaller the litter, above 12 or below 4, the greater the percentage of stillbirths that occurred.⁶ The number of stillbirths increased as the duration of parturition increased from one to 8 hours and as the age of the sow increased. Most of the dead pigs, 80 to 85 percent, were born late in the act of parturition. In large litters deaths might have been due to delays in birth associated with exhaustion of the sow or uterine inertia and anoxia of the fetus due to intrauterine rupture of the umbilical cord. In small litters the larger-sized fetuses presented may have resulted in slower expulsion. Administration of oxytocin to hasten farrowing did not reduce the mortality. If parturition is more than 6 to 7 days early or late the incidence of stillbirths increase. Weak pigs at birth may be due to hypoxia and may be revived by artificial respiration and small amounts of supplemental oxygen.^{6,15} Sows that are anemic, with hemoglobin levels below 9 gm/100 ml, have a higher incidence of stillborn pigs. Iron supplementation during pregnancy is indicated in these sows. Induction of parturition with prostaglandins so attendants may be present to supervise births has reduced the incidence of stillbirths. After about one-half or two-thirds of the litter has been born administration of frequent small doses of oxytocin or the single injection of neostigmine (5 mg/sow)^{6,15} increases the speed of farrowing and reduces the number of stillbirths.

Sows in late pregnancy were exposed for 48 to 96 hours to various atmospheric carbon monoxide concentrations such as might occur in poorly maintained gas-fired heaters in farrowing houses. There was a close correlation between the rates of stillbirths (8 to 80 percent) and the concentrations of carbon monoxide (200 to 350 ppm).^{4,17} Gross lesions in the stillborn pigs were cherry-red discoloration of subcutaneous tissues, muscles and viscera and a serosanguinous pleural effusion. Other distinctive microscopic lesions were also described.

Abortion in Swine

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ABORTION IN SHEEP AND GOATS

Abortions in sheep and goats, as in other larger domestic animals, are due to a wide variety of infectious and noninfectious agents. Because of the methods of breeding and management of sheep in flocks, many animals are at the same stage of pregnancy at the same time and exposure of pregnant ewes to introduced infectious diseases is favored. When an abortion outbreak does occur in a flock it is usually possible to secure 2 to 5 or more fresh fetuses and their placentas for examination and laboratory diagnosis. For this reason, the percentage of confirmed or accurate diagnoses for abortions in ewes is higher than in cattle, about 40 to 60 percent. In most flocks an incidence of 1 to 5 percent abortion and stillbirth is considered "average" or acceptable.¹³ Higher rates of abortion or stillbirth should be carefully investigated. For this purpose fresh fetuses and placentas from aborting ewes should be collected in a clean container, chilled and promptly transported to a well-equipped diagnostic laboratory.

Infectious Causes of Ovine and Caprine Abortion

Bacterial Causes

Campylobacteriosis, Vibrionic abortion (vibriosis) due to *Campylobacter fetus* var *intestinalis* is the most common cause for epizootic ovine abortion in the United States.^{2,4,5b,8,10} *Campylobacter* abortion is rare in goats.^{5,11} It is a cause of serious economic losses in bands of sheep in the Rocky Mountain states and elsewhere in the U.S. It is widespread, occurring in nearly all the sheep-raising areas of the world. The *C. fetus intestinalis* organism in sheep is similar to *C. fetus venerealis* in cattle in some bacteriologic and morphologic characteristics. The former organism in sheep seldom spreads to or infects cows under natural conditions. *C. fetus intestinalis* (*C. jejuni*) can cause abortions in humans so it is of public health significance.⁸

C. fetus intestinalis is catalase positive and H₂S positive; while *C. fetus venerealis* is catalase positive and H₂S negative. The former will grow in 1% glycine while the latter will not. These organisms may be confused with nonpathogenic vibrios, *C. bubulus*, which is catalase negative and *C. fecalis* which is catalase positive but resembles *C. bubulus*. There are 5 whole-cell serotypes (I–V) with two serotypes I and V (C) causing most outbreaks.^{5,8,3} In recent months an intestinal strain of campylobacter called *Campylobacter jejuni* has been

recovered from feces from a number of species including ducks, goats, sheep, cattle, dogs and humans. In these species it may cause an acute diarrhea and in sheep and goats it causes abortions in late pregnancy. *C. jejuni* and *C. fetus intestinalis* are possibly identical, based on serological and cultural characteristics.^{1b,4b,11b}

In affected flocks the incidence of abortion due to vibriosis varies from 5 to 70 percent, with an average of 20 to 25 percent with deaths in about 5 percent of the affected ewes.^{8,2} These authors reported that the disease was observed uncommonly in flocks kept on range the year around, but that it was more commonly seen in sheep kept in feed lots for a part of the winter especially if sanitation was poor. Ewes will frequently smell of and lick aborted conceptuses of other ewes. The disease has been transmitted orally by feeding infective material from aborting ewes as well as by intravenous injection of cultures of *C. fetus intestinalis*. Following oral exposure of susceptible ewes, a period of bacteremia of 7 to 14 days follows as in brucellosis.^{8,11} Under natural conditions infection is probably introduced into clean flocks by carrier sheep that may carry the organisms in their intestines or gall bladder, whether they aborted or not, and shed them in their feces for weeks or months. Carion birds such as magpies and crows may also carry the organisms in their gut from one flock to another.^{13,16,17} *C. fetus* is rather easily destroyed by sunlight, heat or drying, but may remain viable for some time at low temperatures in moist surroundings. This may partly account

Table 12. Summary of the Causes of Ovine and Caprine Abortion

Infectious causes

Bacterial causes—*Campylobacter fetus* var. *intestinalis* and *jejuni*; *Listeria monocytogenes*; *Brucella melitensis*, *abortus*, and *ovis*; *Salmonella abortus ovis*, *dublin*, *typhimurium* and others; *Leptospira pomona* and others; *Corynebacterium pyogenes*, *pseudotuberculosis* and others; and *Pasteurella tularensis*, *pseudotuberculosis* and others.

Miscellaneous bacterial causes—*E. coli* and other coliforms, streptococci, staphylococci, *Clostridium fesi*, *Bacteroides fragilis* and *Mycobacterium paratuberculosis*.

Viral and rickettsial causes—Enzootic abortion (EAE) due to *Chlamydia psittaci*

Miscellaneous viral and rickettsial causes—Tick-borne fever, Wesselbron virus, Rift Valley fever, Nairobi sheep disease, rinderpest, foot and mouth disease, bluetongue, *Coxiella (Rickettsia) burnetii*, Akabane virus and Border Disease and/or BVD-MD virus.

Mycoplasma causes—*M. agalactiae*, *M. mycoides* var *capri* and ureaplasma.

Mycotic causes—*Aspergillus fumigatus*.

Protozoan causes—*Toxoplasma gondii* and *Sarcocystis* spp.

Noninfectious Causes

Drugs, chemical and plant poisonings—phenothiazine, tetramisole, carbon tetrachloride, lead, nitrate, locoweeds, lupines, Veratrum, and onion grass.

Hormonal—estrogens, progesterone deficiency, cortisol and ACTH excess, prostaglandins, and stress.

Nutritional—Deficiency of TDN, copper, cobalt, iodine, selenium, vitamin A and manganese, debility and parasitisms.

Miscellaneous—chromosomal or genetic lethals, severe physical stress, possibly twinning or greater multiples.

for the higher incidence during the winter months.

Vibriosis in sheep in contrast to vibriosis in cattle is not a venereal disease. The ram is not a factor in the transmission of the disease except as he may be an intestinal carrier of the infection.^{4,7} Infertility due to embryonic deaths is not present in ewes mated to experimentally infected rams. The disease is transmitted from infected or aborting sheep to susceptible pregnant ewes the third through the fifth month of gestation. Pregnant ewes infected prior to the third month of gestation do not abort.² There is an incubation period of 7 to 25 days. During the bacteremic period the vibrio enter the maternal placenta where inflammatory changes occur with extension of the infection to the fetal placenta and chorion. The organisms are then carried to the fetus by the placental circulation causing fetal bacteremia.⁸ Abortions may continue in a flock for 6 to 12 weeks. In campylobacter abortion there are often no premonitory symptoms. Occasionally the vulva will swell and a slight reddish discharge may be present. The fetuses are usually expelled the last trimester or 4 to 6 weeks of pregnancy. Abortions occur 1 to 3 days after the death of the fetus. In some cases lambs may be expelled prematurely as stillbirths or at term but die soon after birth. At the time of abortion the fetuses are fairly fresh and only seldom are they decomposed or mummified. The aborted fetuses usually have subcutaneous edema and reddish serum in the body cavities due to autolytic changes. The fetal membranes, especially the cotyledons, show inflammatory changes characterized by edema and necrosis. About 5 percent of aborting ewes may die due to secondary uterine infections, macerating fetuses and peritonitis.^{8,2} About 20 to 60 percent of the fetuses have characteristic necrotic areas or infarcts 1/2 to 3 cm. in diameter in the liver. These contain large numbers of organisms. The cotyledons may be necrotic and organisms may be recovered from these placental structures. **C. fetus** may be identified by stained smears or cultures from the fetal stomach, lungs, cotyledons or uterine exudate.⁸ The latter is usually necessary for a positive identification. The agglutination test on the blood has been of very limited value in the diagnosis of the disease. Fluorescent antibody technique may be of value in the rapid diagnosis of the disease.^{1,2}

Most workers agree that sheep that abort one year are usually immune the second and possibly the third year and carry their lambs normally, but immunity is probably not permanent.^{9,10} In some flocks the disease may appear two years in a row but usually the incidence is much lower the second year. Aborting ewes should immediately be removed from the rest of the flock and isolated for 2 to 4 weeks until genital discharges cease. The

fetus and membranes should be buried or destroyed. Disinfection with a cresylic compound of the infected pen or area after an abortion is desirable.¹

Other precautionary sanitary measures to prevent the contamination of feed and water by infective material is indicated. Injection of 300,000 units of penicillin and 1 gm. of dihydrostreptomycin intramuscularly for 2 daily doses or the daily feeding of 80 mg of chlortetracycline in grain until lambing if done in the early stages of an outbreak of vibriosis will reduce the incidence of abortion about 10 percent.^{6,12} Feeding of antibiotics was not highly effective unless started prior to an outbreak.¹⁰ Although additional injections of antibiotics might be indicated, it is probably not practical.

C. fetus intestinalis serotypes I and V (C) are the most common causes of ovine vibriosis. Cross immunity between these two serotypes does not occur.¹⁰ Two injections 15 to 30 days apart of a commercial bivalent, alum-adsorbed, killed bacterin before breeding or during the first half of pregnancy provided an excellent immunity if done at yearly intervals.¹⁴ Susceptible replacement ewes should also be vaccinated when entering the flock.¹⁵ Recent work has shown that an oil adjuvanted bacterin produced an immunity that lasted for 3 years.¹⁰ Vaccination has been recommended in outbreaks of ovine vibriosis. Since 10 to 14 days are required for immunity to develop, early and prompt diagnosis and administration of the vaccine is indicated for even fair results to be obtained.⁵ The combination of bacterin and antibiotic injections may be used. This disease is rare in does.¹¹

Listeriosis caused by *Listeria monocytogenes* is a worldwide disease affecting a variety of species including man with the septicemic, the encephalitic or the reproductive or abortifacient forms of the disease.^{8,12} It is uncommon to see more than one of these forms in a group of animals at one time. The septicemic form occurs most commonly in newborn or very young ruminants even though the dam may appear normal. The encephalitic form is most common in sheep and cattle. The reproductive form occurs naturally as an epizootic outbreak in occasional flocks of pregnant ewes and does. *Listeria* is a cause of habitual abortion in women. Humans can contract this disease from animals; thus it is of public health significance.

Listeriosis in sheep due to *Listeria monocytogenes* is a much less common cause of abortion than **C. fetus**. In flocks experiencing listerial abortion outbreaks, sheep were recently purchased from flocks where listeriosis had previously been demonstrated.¹² Apparently the disease can be carried latently by clinically normal sheep and excreted during periods of stress. The disease may spread from cattle to sheep on the same farm. Nearly all cases

of ovine and caprine abortions due to listeria will follow by 1 to 3 weeks some radical change in management that caused a lowering of the animal's resistance such as withholding food and water, feeding poor silage in which *Listeria* organisms might have multiplied,^{2,3,10} or heavy feeding to condition ewes for show. The incidence of abortions due to listeriosis varied from 1 to 25 percent which is lower than in vibronic abortion. Abortions usually occur late in gestation and may take place over a period of several months. A few fetuses may be aborted at an earlier stage of gestation. Sheep showing the encephalitic form of listeriosis may rarely also be observed in the flock. The mode of spread is not known but experimental abortions were produced by oral administration of the organisms.^{2,3,10} Intravenous injections of *L. monocytogenes* regularly produced abortions in 7 to 12 days.⁹ The fetuses had usually been dead for several days before expulsion. Thus autolysis and decomposition of the fetus and membranes were often present. Retained placentas were common and associated with metritis.^{2,5} Placental lesions and fetal lesions were not distinctive.⁶ However, listeric abortions resulted mainly from a placentitis.⁵

Postmortem examination of the fetuses revealed evenly distributed small foci of necrosis in the liver and edema and congestion of the meninges. Some lambs near term may be born alive but die within several days with keratitis and liver necrosis. *Listeria* may be recovered by culture from the placenta, brain, abomasum, meconium and other fetal organs.² The genital tract of infected ewes sheds organisms in the uterine discharge for several days after the abortion. Isolation of the organism may be difficult and require repeated cultures of large amounts of refrigerated material (See listerial abortion in cattle). The uterus is usually free of organisms 2 to 3 weeks after abortion. It is assumed that after one abortion the ewe is immune inasmuch as second abortions or consecutive yearly flock outbreaks due to *L. monocytogenes* have not been reported. The fluorescent antibody technique is a helpful aid in diagnosis. Serological tests have been tried with only limited success.^{13,7}

Treatment would logically call for division of the flock into small units, isolation of aborting or convalescent ewes, and proper sanitation and disinfection of premises. Silage feeding should be discontinued. Environmental stresses should be eliminated. Purchase of ewes should be confined to flocks free of listeriosis. Preliminary studies on various types of vaccines have been performed⁸ but none have been developed commercially. The value of antibiotics in an epizootic outbreak has not been determined but could be of value.¹¹

Brucellosis due to *Brucella melitensis*, *Brucella*

abortus or ***Brucella ovis*** is presently rare in the United States as a cause for abortion in sheep and goats. There are no published reports of ***Br. ovis*** abortions in goats.¹¹ In certain areas in and around the Mediterranean region of Europe and Africa, in Russia and possibly Central and South America brucellosis due to ***Br. melitensis*** is an enzootic and a common cause for abortion, especially in goats.^{4,5,8,9} Ovine abortion due to ***Brucella melitensis*** has not been reported in recent years in the United States. An outbreak of ovine abortion due to ***Br. abortus*** in Minnesota apparently contracted from infected cattle was reported. Infections and abortions persisted in this flock for more than 40 months.^{10,11} This was apparently a rare occurrence as sheep are quite resistant to ***Br. abortus***.^{10,13} The third form of brucellosis, due to ***Brucella ovis*** (ram epididymitis organism) (REO) has been reported in Australia and New Zealand, Central Europe, S. Africa and the United States where its principal pathologic effect has been in rams causing infertility. In California the incidence of infected rams was 20 to 25 percent.¹⁰ Abortion in ewes due to ***Br. ovis*** is of little importance and is seldom reported except in New Zealand where an incidence of 7 to 10 percent was noted in some flocks.^{5,14}

In brucellosis in goats due to ***Br. melitensis*** the incidence of abortion may reach 40 to 60 percent. Abortions occur the last third of gestation and weak moribund kids or lambs may be born at term or prematurely. Like brucellosis in cattle the disease is contracted by pregnant sheep or goats by ingestion of food and water contaminated with organisms from aborted fetuses and their membranes or genital discharges. After intravenous inoculation of ***Br. melitensis*** abortions may occur 10 to 21 days later. A placentitis involving the placentomes with necrosis of the chorioallantois occurs in advanced cases. The fetus is also infected with inflammatory and necrotic foci in the liver and other organs.^{2,15} Diagnosis of the disease is based on cultures of aborted fetuses or stillbirths and serologic tests, the most useful of which is the agglutination test. Following abortions or infection some ewes or does may carry the infection for months, years or a lifetime in various organs, especially the udder and uterus.^{11,12}

Control of the infection is patterned after the control of brucellosis in cattle and swine. Sanitation, blood testing by the tube agglutination, CF and card tests,^{5,11} isolation or quarantine and slaughter are necessary. Agglutination titers of 1:25 are positive. Milk tests such as the whey agglutination test have not proven as satisfactory for the diagnosis of brucellosis in goats as in cattle. As in swine serologic tests may be unreliable in individual goats but on a herd basis even one positive sample indicates a herd infection.^{5,11} Vaccines have been tried in

the control of **Br. melitensis**. **Br. abortus** strain 19 vaccine is of questionable value. Two other vaccines have been more effective; one is an oil and water adjuvanted killed vaccine of **Br. melitensis** that produces a severe local reaction and persistent titers and the other is an avirulent living **Br. melitensis** vaccine (Rev 1) recommended for use in sheep and goats at 3 to 8 months of age.^{5,11,6,7} Vaccination is not practiced in the United States since the incidence of **Br. abortus** and **melitensis** is extremely low.

In brucellosis due to **Br. abortus** in sheep and goats the signs, lesions and diagnosis are similar to those with **Br. melitensis**. The disease may rarely spread from infected cattle to pregnant sheep or goats and cause abortions the last third of gestation. The occurrence of this form is rare. It should be controlled promptly in a manner similar to brucellosis in cattle, except for vaccination. Isolation, quarantine and slaughter procedures are recommended.

Brucellosis due to **Br. ovis** in ewes is lower in pathogenicity than **Br. melitensis** or **Br. abortus**. Ewes abort only if infected during pregnancy especially the first or second month of pregnancy since it requires 1-1/3 to 3 months or more to produce severe enough lesions of edema and coalescing areas of necrosis in the placenta and intercotyledonary placenta to interfere with fetal nutrition and result in the death of the fetus and abortion or the birth of weak diseased lambs.^{9,13,16} Apparently ewes are difficult to infect with **Br. ovis** unless they are pregnant. Breeding ewes with infected rams seldom causes the disease in ewes. Ewe to ewe passage of infection is rare. Ram to ram infection occurs most commonly by a susceptible ram breeding a ewe recently bred by an infected ram and contaminating his prepuce with the **Br. ovis** organism. Oral infection from pasture, feed, or water contaminated with material from aborted fetuses, membranes or genital discharges can occur but is of little importance. The disease can be produced in pregnant ewes by the inoculation of the conjunctival, nasal or rectal mucous membranes or by parenteral injection.^{8,9} Since intravaginal deposition of infected semen, as in cattle, seldom produces the disease it has been suggested that intrarectal ejaculation of infected semen or sodomy may be a means of spread of this form of ovine brucellosis from ram to ewe or ram to ram.⁸

The incidence of abortion due to **Br. ovis** is low.^{2,4,8,9,13,14} New Zealand workers⁵ indicated a high incidence of 7 to 10 percent in 40 naturally-infected flocks. Abortions usually occur the last trimester of pregnancy. Chronic placental lesions of necrotic plaque-like thickening and edema of the intercotyledonary areas of the placenta is characteristic of **Br. ovis** infection.^{9,16} Smears

of these areas stained with Stamp's modification of Ziehl-Neelsen stain often reveal the organism.¹⁴ The organism may be cultured from the fetus, the membranes and the uterine discharges for a week after abortion or premature lambing. The complement fixation (CF) test is a highly satisfactory serological test for determining the presence of **Br. ovis** in a flock or individual.¹⁰ The fluorescent antibody technique may also be used to detect **Br. ovis** in contaminated material in the placenta or semen. Infection in ewes persists from one breeding season to the next in only a few ewes.⁸ However, rams may be chronically infected for 3 or more years. There is no evidence that lambs born from infected ewes retain infection. There is little evidence **Br. ovis** causes infertility in ewes. Infertility in rams is the major cause for losses from this disease. Since the effects of **Br. ovis** infection in the ewe are limited and the infection is transient, most control efforts are aimed at the rams. Palpation of the testes for the presence of lesions, especially in the region of the cauda epididymis will clinically diagnose most individual infected rams. The use of the CF test on all rams will detect clinically and nonclinically infected males. Repeated clinical and serological testing and the elimination of infected rams will rapidly reduce the infection rate and eliminate the infection in a flock. Replacement rams should be raised or purchased from disease-free flocks and tested prior to and after a 2 to 3 months isolation period. An effective vaccination procedure for young rams combining the simultaneous use of **Brucella abortus** Strain 19 and a formalin-killed oil adjuvant **Br. ovis** vaccine has been used widely in Australia and New Zealand.¹ A vaccination procedure consisting of injecting an alum-precipitated **Br. ovis** bacterin subcutaneously in 2 doses 30 to 60 days apart and followed by a single injection each year has been used in California.³ Because of the nature of the disease it is probably unnecessary to vaccinate ewes.⁹ Antibiotic therapy, especially in chronic cases, is of doubtful value.⁶

Salmonella (paratyphoid) abortion in sheep is principally caused by **Salmonella abortus ovis**, **S. typhimurium** and **S. dublin** and others.^{8,11,1,4,6} **Salmonella** spp. infections have caused outbreaks of abortions in goat herds.¹¹ These are uncommon and detailed clinical reports are not available. This type of infection has been described in England and Europe, especially Germany, but not in the U.S. The incidence of abortion varied from 8 to 60 percent.^{10,6} The infection is contracted orally by contamination of feed and water with aborted material or organisms from other common animal sources. An outside carrier animal added to the flock may introduce the disease. Stress situations often precede an outbreak.^{8,2} In a few cases diarrhea or other evidence of

infection of the ewe such as high fever and depression has been noted but in most cases no signs other than abortions in the last third of gestation or stillbirths at term are observed. Occasionally deaths may occur in newborn lambs and 5 to 7 percent of affected ewes.^{8,5}

The organisms are readily isolated from the internal organs of the fetus, the placenta, and the uterine discharges for a few days after abortion. An agglutination test can demonstrate antibodies in the blood serum of infected ewes or rams. Aborting ewes should be isolated and aborted fetuses and placentas should be destroyed. Contamination of feed and water must be prevented. Rodent control is essential. Although autogenous bacterins have been used very early in an outbreak, or as a preventative in reducing the incidence of abortion, their use has not been scientifically evaluated. Individual ewes may benefit from antibiotics, 10 mg/kg tetracycline daily, and supportive fluid therapy.^{8,10,2}

Leptospirosis due to *L. pomona* and *L. icterohemorrhagiae* and others is seen much less frequently in sheep and goats than in cattle and swine as they appear more resistant to infection. The disease is more common in young lambs than in older ewes.^{5,8,10,11,4}

Leptospirosis as a clinical disease of goats has been reported infrequently. Outbreaks of leptospirosis in older pregnant ewes that caused abortion in up to 20 percent of the flock have been described.² Other symptoms included icterus, hemoglobinuria and death of the ewes. An outbreak of abortion in goats due to *L. grippotyphosa* was reported in Israel.¹ Based on experimental infections, sheep may have a leptospiruria for 40 to 100 days.⁵ No fetal infections were observed before 21 days after intraarterial inoculation of *L. pomona*. *Leptospira* may be cultured from fresh fetal or placental material, and seen by histologic or fluorescent antibody (FA) techniques.⁸ In autolyzed fetal or placental tissues cultural methods may be unsuccessful. As in cattle and swine, serologic tests are of limited value in the diagnosis of the disease. Treatment of the disease with an inactivated vaccine, usually multivalent, and antibiotics should be conducted along lines similar to those employed in cattle.^{11,3}

Miscellaneous Bacteria Causing Ovine and Caprine Abortion

Pasteurella tularensis and *P. pseudotuberculosis* are sporadic causes of abortion in ewes the latter part of the gestation period.^{5,10,13,4} The latter organism was reported¹³ to produce white necrotic foci in the liver of fetuses. Tularemia due to *P. tularensis* is common in western

United States where it causes enzootic outbreaks of disease in wild rodents and can be transmitted to sheep by the common wood tick, *Dermacentor andersoni* and other ticks. Man is also susceptible to infection. The disease has been described in Europe and Japan. Affected sheep show depression, anorexia, elevated temperature, increased pulse and respiratory rates, coughing, premature births, stillbirths and abortions. One attack confers a long-lasting immunity with a persisting antibody titer. The agglutination test on the serum is useful for diagnostic purposes but may cross react with *Brucella* organisms. Injections of streptomycin or oxytetracycline produced a prompt clinical response and reduced losses. Controlling tick infestation of sheep by dipping or by keeping sheep from infected ranges is indicated.⁴

Cornynebacterium pyogenes, *C. pseudotuberculosis* and even *C. renale* and *C. equi* have been recovered from aborted ovine fetuses. *C. pyogenes* is the most common strain.^{1,3} This organism may also cause deaths in newborn lambs.

Other miscellaneous bacteria causing abortion in ewes include: *E. coli* and other coliform organisms, streptococci and staphylococci.^{9,13} Blackleg of the fetus due to *Clostridium fesi* infection following shearing wounds resulted in death of the fetus and distension of its tissues and the uterus and abortion.^{1,10,2} *Bacteroides fragilis* was described as a cause of abortion in ewes,^{13,5} as was an organism resembling *Bacillus cereus*.⁶ Johne's disease or *Mycobacterium paratuberculosis* in goats is a chronic condition resulting in debility, failure of conception, abortions and births of weak kids. There is no effective treatment.¹¹

Viral and Rickettsial Causes of Abortion in Ewes and Does

Enzootic abortion of ewes (EAE) chlamydiosis or ovine virus abortion is caused by a viral agent of the psittacosis-lymphogranuloma (PL) group (*Chlamydia psittaci*). There is good evidence that the agent causing epizootic bovine abortion, EBA, and EAE are the same.^{5,6,8,11,2,6,12} Enzootic abortion of ewes and goats has been described in Scotland and England, Europe and in Western United States. In these latter states EAE or chlamydiosis is a common occurrence in sheep and goat flocks.^{5,8,10,16} Chlamydial viruses have also been described as causing pneumonia and polyarthritis in sheep and goats.^{5,8,11,10,13} Latent persistent chlamydial infections of the ovine and caprine intestinal tract are common.^{5,10,11} Further study is necessary to determine the relationship of these chlamydial agents to each other and

to abortion in ewes and goats. Evidence indicated that all these agents caused abortion in experimental ewes. Ewes with latent intestinal *Chlamydia* spp infection showed no increased resistance to superinfection and often aborted when challenged.¹¹ The causative agent is an obligate intracellular parasite that forms elementary bodies.⁵ Chlamydiosis is characterized by abortions from 100 days of gestation to term but most commonly the last month of pregnancy. Occasionally macerated or mummified fetuses are observed. The birth of dead fetuses or weak, moribund lambs and kids is not uncommon. One fetus of twin lambs may be affected. The incidence of abortions in a flock where the disease is enzootic, is usually 1 to 5 percent but in susceptible flocks the incidence may reach 30 percent. Most abortions occur in two- and three-year-old ewes in the chronically-infected flocks. Retained placenta may occur and be associated with a brownish genital discharge. Occasionally ewes and does may die from metritis and other complications after abortion. Most ewes bred satisfactorily following abortion as an immunity was developed.^{8,10,13,12} The disease may be difficult to differentiate from campylobacteriosis (vibriosis). In fact, occasionally both infections may occur concurrently in a flock.³ This chlamydial agent causing abortion in sheep and cattle also causes abortion in goats.^{5,11,1,9}

Enzootic abortion of ewes (EAE) or chlamydiosis due to *Chlamydia psittaci* can be produced by oral feeding of the agent to susceptible ewes and does. The incubation period is about 50 to 90 days.⁸ Infection is probably most commonly due to ingestion of feed or water contaminated with infective material from aborting ewes and does. Although rams may become infected as determined by the CF test on serum there is no indication they are implicated in the spread of this disease. Ewe lambs or does born in infected flocks may later show evidence of disease during pregnancy. Susceptible ewes or does contracting the infection at one lambing period may abort during their next pregnancy. The disease is not tick-born.

The fetal membranes are grossly similar to the fetal membranes present in bovine abortions due to *Br. abortus*. The chorionic membranes and cotyledons are thickened, edematous, necrotic and leathery and often retained. The aborted fetuses usually show signs of autolytic changes that are not distinctive. Staining of placental smears and examination with the microscope usually demonstrate the elementary coccoid viral bodies in the epithelial cells. The fluorescent antibody test is reliable but staining is just as reliable and easier.^{5,8,11} The virus from the fetal membranes may be cultured in chick embryos and mice. Virus is seldom found in the fetus. Vaginal swabs taken soon after abortion are the best sam-

ples for the isolation of chlamydia.⁵ Most ewes and does show a complement fixation titer in the serum from two weeks to 4 months after abortion. The CF test is not highly accurate because some infected individual ewes and goats may show no titers. Other nonaborting ewes may carry a titer due to natural infection or due to the latent agent commonly found in the digestive tract.^{5,8,10,11,13,2}

Workers in Scotland and the U.S. produced a formalized killed adjuvanted vaccine that proved effective as an immunizing agent for EAE. The immunity lasted for 2 to 3 years after a single injection. This vaccine given prior to the first breeding and to susceptible additions to the flock has also proven of value in Idaho and California and federal licensing is expected.^{8,14} Experimentally chlortetracycline fed at a rate of 100 to 250 mg per head per day^{5,11} to exposed or inoculated ewes or does may prevent abortions. Injection of tylosin and tetracyclines might also prove helpful. However treatment is not completely effective. Once the infection was established in the placenta abortions could still occur.

Miscellaneous viral and rickettsial diseases of sheep causing abortion are as follows:

Tickborne fever is due to *Rickettsia phagocytophilia*. It has been reported in the United Kingdom and Scandinavia in goats, sheep and cattle and is transmitted by ticks, *Ixodes ricinus*.^{1,8,12,13} After inoculation of infected blood, fever developed in 4 to 8 days and lasted for 10 days. During this period abortions occurred. When susceptible pregnant animals are moved from tick-free to tick-infested pastures late in gestation abortions may occur in up to 50 percent of the ewes and does and deaths in aborting animals may occasionally reach 20 percent. The causative agent may be found by microscopic examination of the blood in aborting ewes. The inclusion bodies of this organism are seen in the cytoplasm of neutrophils and large monocytes. A complement fixation test has proven to be an accurate diagnostic serologic procedure.¹ Ewes and does reared on tick-infested pastures are apparently immune.⁸

Wesselsbron virus is a cause of abortion in sheep and death in newborn lambs in South Africa.^{12,13,11} A few affected ewes may die. The virus is transmitted by mosquitoes. Antibodies to the virus are present in the serum of sheep after recovery. The virus apparently affects and kills the fetus *in utero* and may be cultured from the aborted fetus. Presently a modified live virus (MLV) vaccine is given annually to all ewes before breeding.⁸

Rift Valley Fever virus or enzootic hepatitis, was a major cause of abortion in Kenya and South Africa in sheep, goats and cattle^{1,8} until a vaccine was developed and used extensively. Signs of abortion and deaths in

newborn lambs resembled disease due to Wesselsbron virus. Occasional deaths occurred in older ewes and goats. This disease is also transmitted by insects. As with Wesselsbron virus the disease may affect man causing an influenza-like syndrome. Viral isolation and serologic tests can confirm a clinical diagnosis of the disease.^{1,8}

Nairobi sheep disease virus in Africa^{12,13} or rinderpest and foot and mouth disease^{2,11} although not present in the United States cause abortions in sheep in countries where these diseases are prevalent.

Bluetongue virus vaccine, a live viral preparation, if used on pregnant ewes, or a natural infection occurs in ewes and goats between the fourth and eighth week of gestation cause up to 20 percent fetal losses characterized by stillbirths, mummified fetuses or spastic neonates with a variety of developmental central nervous system defects.^{1,8,3,7} Goats, like cattle, are occasionally affected by bluetongue virus but are more naturally resistant than sheep.⁸ Bluetongue has been reported in most southern and western states⁶ and in many other countries. It is spread between animals during warm weather by insect vectors, especially the *Culicoides* fly.^{8,10} The viremic stage may last for four months in sheep even though neutralizing antibodies are in the blood. Cattle may also harbor the virus and be a factor in the spread of the disease to sheep.⁴ Bluetongue (MLV or inactivated) vaccines are now available but since there are a number of serotypes of bluetongue virus a heterologous vaccine would be more effective than the homologous vaccine presently used.^{1,8,6}

Coxiella or Rickettsia burnetii or Q fever virus has been recovered from the placenta of cattle, ewes and goats in North America, Australia and Europe. In several flocks abortions occurred and antibodies were found in the blood of ewes and *Coxiella* organisms were recovered from the placenta.^{1,8,11,1,12} This rickettsial agent was not highly pathogenic for sheep and goats and seldom was a cause for abortion.^{12,9} Positive serologic tests and cultures are common where Q fever virus is endemic, even in ewes, goats and cattle having a normal birth and offspring. However when outbreaks of abortions occur in sheep and goats and this rickettsial agent is found culturally and serologically and no other cause for the abortions can be ascertained, veterinarians will believe this is the probable cause of the abortions. Possibly when infections are severe abortions can result.^{1,12}

Akabane virus causing fetal arthrogryposis and hydranephaly described previously in cattle (Chapter III) also affects ovine and caprine fetuses. It has been reported in Japan, Australia and Israel. The virus is transmitted by *Culicoides* insect vectors. It may also cause abortion, premature birth or stillbirths.¹

Border disease, "Hairy Shaker" Disease, Hypomyelinogenesis congenita in sheep and goats is caused by a virus closely related to or identical with BVD-MD and hog cholera viruses. It has been reported in the United Kingdom, New Zealand, Australia and Europe^{1,8,11} and possibly in the United States.⁵ Affected pregnant ewes and does may abort or produce defective newborn. Hair coat defects common in sheep are not observed in newborn kids with signs of CNS disease.¹¹ Pregnant sheep and goats should be separated from cattle⁸ as cattle shedding virulent BVD-MD virus in large amounts may infect pregnant ewes and does. Two studies^{5a,b} reported on "Border Disease" in California and northwest United States based on serologic tests for BVD-MD virus in ewes and lambs and the recovery of the virus from the nasal and vaginal cavities of ewes and experimental reproduction of the disease. However Ward in 1971¹³ and English workers in 1980¹⁰ showed that the inoculation of BVD-MD virus into pregnant ewes from 22 to 105 days and 25 to 40 days of gestation, respectively, resulted in 40 to 70 percent "empty" ewes at the time of lambing, up to 40 percent abortions, a few mummified fetuses and a number of stillbirths and neonates exhibiting growth retardation with hypomyelinogenesis, cerebellar hypoplasia and hydrocephalus. Border disease virus may be recovered from infected newborn fetuses and the dams' genital tract in the early postpartum period.^{1b} Border disease was produced in lambs following the artificial insemination of their dams with semen from persistently infected rams. Certain infected rams and ewes producing infected lambs may not have circulating antibodies to BD virus. There were marked differences between strains of BD and BVD viruses in their antigenicity.^{1b} Further studies are indicated on the very close relationship of BD and BVD viruses and the similar disease conditions produced in sheep and cattle.^{5b}

Inoculation of the **ovine progressive pneumonia virus (OPPV)** into the fetal amniotic sac at 45 to 85 days of gestation caused resorption, maceration or abortion of the fetus. Inoculation after 100 days of gestation had no clinical effect but the healthy lambs could be carriers of OPPV.^{1a}

Mycoplasmal and Fungal Abortions

Mycoplasma agalactiae causing mastitis (contagious agalactia), arthritis and keratoconjunctivitis in sheep and goats may occasionally be associated with vulvovaginitis and abortion.¹¹ **Mycoplasma mycoides var capri** and other mycoplasma have been isolated from goats and sheep in the United States.³ Although the former mycoplasma causes contagious caprine pleuropneumonia, myco-

plasma have been recovered from esophageal-pharyngeal fluids from dead fetuses from does. *Ureaplasma* spp has been associated with infertility and abortion in sheep in Texas.²

Aspergillus fumigatus, a fungus, has been described only occasionally as a cause for abortion in ewes and goats.¹

Parasitic Protozoal Infections Causing Abortions

Toxoplasma gondii, a protozoa, may infect all domestic animals but only in sheep and goats is it a common and serious cause of abortion. Toxoplasmosis occurs widespread throughout the world and in the United States and Canada. The infective form of *Toxoplasma gondii* is found as a coccidial oocyst in cat feces resembling that of the coccidia.^{1,5,8,11,12,4,5,6a,b,7,8,11} Experimental infections have been produced by inoculating infective material.¹¹ Control of the cat population on the farm may help prevent toxoplasmosis in sheep and goat flocks. The presence of cats on small farms make this disease more frequent in small flocks than in large range flocks.⁸ Natural outbreaks in goat flocks are uncommon.^{1,8,4} Heavy rainfall favors the spread of the disease. Stress may cause latent toxoplasmosis to become active. Occasional cases of congenital or intrauterine infections of the newborn have been described in most species of domestic animals. If antibodies are present in the dam no transmission of the infection to the fetus occurs.^{1,13} The importance of toxoplasmosis as a cause of early fetal resorption, maceration, mummification, abortion and neonatal deaths varies in different countries. In New Zealand 50 to 60 percent of abortions and neonatal deaths were due to this disease; in Yorkshire, England about 15 percent and in the U.S. only sporadic outbreaks have been reported. The incidence of abortion in a flock may vary from 3 to 30 percent. Ewes and does infected prior to breeding do not abort. Those infected from 30 to 90 days postbreeding usually have fetal resorption or mummification. Most observed abortions occur the last trimester of gestation, 2 to 3 weeks before term after infection during the latter half of gestation. The incubation period from the feeding of sporulated oocysts to abortion in sheep was 28 to 34 days.¹ One normal twin and one dead twin may be born at term. Ewes aborting due to toxoplasmosis often have a retained placenta. Affected ewes bred back and produced normal lambs the next season. Chronically infected ewes do not have abortions or diseased newborn as do acutely infected pregnant ewes.^{1,11,13} Stillbirths, living, defective, ataxic, weak and dull lambs and normal lambs, as well as aborted fetuses may carry *Toxoplasma gondii*. This organism produces a characteristic

placentitis with multiple small, 1 to 3 mm., soft white nodules amongst the fetal villi in the dark red caruncle or cotyledon. (See Figure 70.) The organism is readily identified either free or in cysts. The intercotyledonary placenta is often edematous. Fetuses or stillbirths show no gross lesions but organisms may be recovered from the liver, lungs, or brain.

The Sabin-Feldman dye test or the indirect hemagglutination method on ewe's or doe's blood detects antibody usually present at the time of abortion and the titer continues to rise for several weeks. The CF test and skin sensitivity test have also been used but the latter is of less value in the diagnosis of toxoplasmosis.^{10,12,13} The indirect fluorescent antibody test on imprints of fresh cut tissues has proven valuable.¹ Occasionally campylobacteriosis (vibriosis) or other causes of abortion are found associated with toxoplasmosis. There is no satisfactory treatment for this disease. Sulfonamides and pyrimethamine have been tried.¹ It should be noted that animal to man transmission of toxoplasmosis can occur and acute infections in pregnant women should be prevented as the organism has a great affinity for the human fetus.^{10,14} Vaccination with a nonpathogenic coccidium may prove of value to protect susceptible ewes and does against toxoplasmosis.⁵ A recent review of toxoplasmosis in humans has been published.¹⁵

Sarcosporidiosis (Sarcocystosis) caused by *Sarcocystis* spp is similar to the life cycle of toxoplasma except most carnivores can excrete the various protozoal oocysts. Sarcosporidial cysts can be found in striated muscle in sheep and goats. *S. ovis* is a parasite in the dog's intestinal tract which when ingested in large numbers by susceptible sheep or goats results in anemia, anorexia, ataxia and abortions during the period when the vascular endothelium is parasitized by schizonts.^{5,2,3,9,11,12,13b} Large experimental infections induced in pregnant ewes caused premature births and deaths of the ewes. Their lambs did not have congenital sarcocystosis.^{13b} (See swine.) Sarcosporidiosis is distributed world-wide. The *S. tenella* infection in cats can be passed to sheep but apparently it is nonpathogenic.² *Globidiosis* caused by the coccidia *Eimeria* (*Globidium*) *gilruthi* and *Besnoidia* may be transmitted in a manner similar to the above parasitic protozoa. There is no good evidence however, that they cause prenatal or neonatal deaths in fetuses or newborn domestic animals.

Noninfectious Causes for Ovine or Caprine Abortion

Drugs, Chemical or Plant Poisonings:

Although the following causes of abortion in ewes and does have been reported, some of these causes are prob-

ably questionable and require further documentation and experimentation to ascertain their significance. Some abortions may be due to a combination of causes of which only one was recorded.

Phenothiazine administered to ewes in late pregnancy may cause abortions within 4 days postworming.²⁶ The author has observed dead, emphysematous, macerating fetuses causing severe dystocia, metritis and death following this practice. This may be due to the stress of handling rather than the drug. Tetramisole and phenothiazine, but not thiabendazole has been reported to cause abortion in goats.¹¹

Carbon tetrachloride, a chemical seldom used currently in parasite control, may cause abortion if administered to pregnant ewes, and goats.^{11,12,13}

Chronic lead poisoning may cause abortion in pregnant ewes.³

Nitrate feeding in doses in excess to that occurring in forage and causing a severe methemoglobinemia may occasionally cause abortion in ewes.¹⁰

Locoweeds (*Astragalus lentiginos*, *A. pubentisimus* and *Oxytropis sericea*) caused abortions in all stages of gestation, and deformed and small weak newborn if fed to pregnant ewes and goats as hay or if grazed upon in pasture.^{11,14,16,17}

Lupine ingestion resulting in chronic lupinosis has been associated with abortions and fetal deaths in ewes as has consumption of **broomweed (*Gutierrezia microcephala*)** by goats.^{11,20} ***Indigofera spicata***, (creeping indigo) caused abortions in sheep.¹⁶

Veratrum californicum (False Hellebore) if consumed by pregnant ewes will cause early embryonic deaths, aborted fetuses and deformed lambs.^{16,23}

Ergot fed to ewes at levels of 0.1 to 0.7 percent of the ration reduced the percent of ewes that lambed by 20 percent.⁷

Onion grass (*Romulea bulbocodium*) when ingested by pregnant ewes may cause abortion.^{12,13}

Hormonal Causes for Abortion in Sheep

Estrogens—The ingestion of excessive estrogens in subterranean clover by sheep in Australia often resulted in uterine inertia, dystocia, and the birth of stillborn lambs.⁴ Dystocia and sterility remained at a rather high level even though the sheep were removed from the clover pasture because of permanent uterine damage by the estrogens. An isoflavone derivative, genistein, was the active estrogen in the clover.⁸ It has estrogenic activity equal to one-fifth that of estrone. In certain fresh-cut subterranean clovers, such as the dwalganup variety,

concentrations of 100 mg. of genistein per 100 gms of clover was found. Small amounts of hexoestrol in the grain ration the last few weeks of pregnancy caused abortion in 11 of 14 ewes.^{12,13}

Progesterone deficiency, or cortisol or ACTH excess has been reported as causes of abortion in goats and sheep. Many Angora goat farms in South Africa had over 30 percent abortions each year.²² The condition did not affect other herds of goats and so it was considered to be genetic in nature. Abortions occurred from 2 weeks of gestation to term with over 60 percent occurring from 100 to 120 days of gestation. Fetuses were partially autolyzed when expelled. A higher incidence was present in the older does. Does conceived promptly after aborting. Abortions were caused by regression of the corpus luteum, necessary in the goat to maintain pregnancy. There was evidence of a lack of luteotrophic hormone from the anterior pituitary gland. Stress, such as shearing, seemed to contribute to an increased incidence of abortion. As discussed in cattle abortion the pituitary-adrenal axis largely controls the onset of parturition in sheep and goats. In habitual abortions occurring in Angora goats²² hyperplasia of the adrenals was observed in aborting does and their fetuses.^{24,25} It was considered that selection for fleece quality in Angora goats raised for mohair production favored animals with adrenal hyperplasia.

If ovine fetuses were given ACTH, corticotropin, or cortisol abortion would occur within 3 to 7 days.^{18,25} If the former hormone was given the fetal adrenals would become as large as those in fetuses at term. Conversely if the fetal pituitary was destroyed or the fetal adrenals removed, prolonged gestation resulted. Injections of cortisol (hydrocortisone) or dexamethasone (Azium) in relatively small doses into ewes in late gestation caused the premature induction of parturition.^{2,25} Larger doses of cortisol administered to ewes during early gestation had no effect but after 85 days of gestation they proved lethal to the fetus.

Prostaglandin F_{2a} at a dose of 15 mg caused abortions in goats at 30 and 65 days of gestation and premature births at 140 or 142 days of gestation.⁵ When the prostaglandin analogue, cloprostenol (Estrumate, ICI) was injected at a dose level of 0.5 or 0.50 ml per goat IM or SC between 72 and 132 days of pregnancy abortions occurred 30 to 50 hours later.⁹

High ambient temperatures and high humidity causing adrenal hyperactivity and hydrocortisone injections shortly after breeding caused increased embryonic deaths.¹⁵ Stress factors and their effect on the pregnant ewe especially in late pregnancy may play a definite role in inducing abortions as in toxoplasmosis, phenothiazine poisoning, and reduction in energy intake or ketosis.

Nutritional Causes of Ovine Abortion

Lack of TDN or energy has been widely reported in England and elsewhere as a cause of abortion. A high incidence of up to 80 percent abortions and/or maternal deaths have been associated with pregnancy toxemia or ketosis in ewes, especially those having 2 or more fetuses, and on a restricted energy intake and lack of exercise in late pregnancy. Ewes fed only roots during pregnancy had a high abortion rate due to the reduced energy intake.^{12,13} Severe parasitism, malnutrition and exposure or a combination of these may induce abortion prior to death of the doe.^{11,20}

Copper deficiency was reported to be associated with stillbirths in ewes.^{12,13} A manganese deficiency has been associated with abortion in does at 80 to 100 days of gestation.¹¹ **Cobalt deficiency** has been reported associated with a high death rate in neonatal lambs.¹⁹

Vitamin A deficiency of long standing caused a high incidence of stillbirths or poorly viable newborn lambs and kids.^{11,12,13}

Iodine deficiency has also resulted in congenital goiter and abortion or stillbirths in sheep and goats.^{11,12,13}

Selenium deficiency in ewes in New Zealand has been reported to cause abortion or neonatal deaths of lambs with congenital white muscle disease affecting the heart. It has been associated with farms having a large number of barren ewes and reduced lambing percentage.^{12,13} Experimental diets high in sulfur caused fetal deaths and abortion with evidence of white muscle disease despite the administration of selenium and vitamin E to the pregnant ewes.⁶ The administration of sulfur probably interfered with the absorption or utilization of selenium. The administration of 5 mg of sodium selenate or selenite monthly for 3 doses before breeding and again one month before lambing was recommended.¹³ A muscular dystrophy in sheep with early neonatal deaths not associated with selenium deficiency has been described.²¹

Chromosomal, physical and miscellaneous causes

Lethal genetic defects causing fetal deaths, abortions and stillbirths have been described previously. (See Chapter III.) Severe physical stress, fright and exhaustion, such as caused by dogs chasing a flock of ewes in advanced pregnancy, has occasionally been reported as a cause of abortions or premature births. Young ewes have a higher incidence of stillbirths than older ewes.^{12,13} Ewes carrying twins or greater multiples especially if on a low protein ration were more apt to abort or have stillbirths than those carrying single fetuses.

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ABORTION IN THE BITCH

Abortions in bitches are much less common than in the larger domestic animals. Most canine abortions are sporadic except for enzootic or epizootic outbreaks in kennels due to **Br. canis**. Limited experimental work has been done on other causes of abortions in small animals.

Infectious Causes of Canine Abortions

Bacterial Causes

Brucella canis is the most common cause of third trimester abortion and infertility in bitches and epididymitis, testicular atrophy and infertility in males,^{8,9c,24} It can be a serious cause for losses in breeding kennels. This highly contagious disease is widespread in the United States and other countries. The incidence of canine brucellosis, based on serologic tests, varies from 1 to 10 percent of dogs in the United States.²⁴ Since serologic tests are inaccurate the true incidence may be much lower. For example in the north midwest states 6.7 percent of 2,572 dogs were positive on the slide test, 1.5 percent^{25,72} on the tube agglutination test and only 0.2 percent positive on blood culture.³ In northeastern U.S. about 0.5 to 1.5 percent of dogs are possibly infected.^{8,24} Although initially observed in Beagles in the late 1960's, it now occurs in all breeds and in both kenneled and free-roaming dogs. The incidence is higher in states and countries where the climate is mild and free-roaming packs of dogs are common.^{7,24} The disease in dogs resembles brucellosis in swine due to **Br. suis** but is relatively mild. **Br. canis** is an intracellular pathogen morphologically similar to other **Brucella**. It cross reacts with **Br. ovis** and rough variants of other **Brucella** as well as **Actinobacillus equuli** and **Pseudomonas aeruginosa**.⁸ Canine brucellosis is characterized by abortion occurring between gestation days 30 and 57 with about 85 percent of the observed abortions occurring between days 45 and 55. Some infected bitches may carry their fetuses to near term and deliver both live and dead pups. The living pups may survive and appear healthy but be bacteremic for at least two months. Up to 30 percent of infected bitches may abort two or three litters in succession. Apparent failure of conception was also commonly ob-

Table 13a. Summary of the Causes of Canine Abortion

Infectious causes:

Bacterial causes—**Br. canis**.Miscellaneous bacterial causes—**Br. abortus** and **suis**, staphylococci, streptococci, pseudomonas, coliform and salmonella organisms.

Viral Causes—Distemper virus, adenovirus (infectious hepatitis) and canine herpesvirus (CHV).

Other infections—**Toxoplasma gondii**

Noninfectious Causes:

Drugs, chemical, poisons—O-diazoacetyl-L-serine, N-desacetyl thiocolchicine, malucidin and others.

Hormonal—progesterone deficiency, prostaglandins.

Physical—severe trauma (?)

Nutritional—manganese deficiency (?)

Miscellaneous—genetic defects, parturient conditions and stillbirths.

served and this was due to early unrecognized embryonic deaths between gestation days 10 to 25.^{8,22,24} Early abortions were largely unobserved because the affected bitches would ingest the expelled membranes and embryos. These early breeding failures may also be repeated three or four times after consecutive breeding periods.²⁴ Occasionally a bitch would abort, have a normal pregnancy and then abort again. The incidence of abortion in a susceptible kennel of dogs may reach 80 percent. Retained placentas were not observed. However, prolonged vaginal discharges were commonly seen lasting from 4 to 6 weeks after an abortion. The living pups often died and some fetuses had degrees of autolytic changes. In adult male dogs epididymitis was a consistent sign and the scrotum was hyperemic, swollen and painful resulting in scrotal dermatitis secondary to excessive licking. The epididymides were enlarged and firm and testicular degeneration and atrophy were often observed. Primary orchitis is seldom noted but the prostate is commonly affected. Semen samples are abnormal with varying degrees of oligospermia to azoospermia and containing many neutrophils and monocytes. Other lesions due to **Br. canis** include lymph node and splenic enlargement, and occasionally discospondylitis and recurrent uveitis.^{7,24} Clinical signs of pyrexia, depression, anorexia are usually absent and deaths due to **Br. canis** have not been reported.^{7,24}

Transmission of the disease can occur by inoculation of fairly large numbers of infective organisms but probably occurs naturally by oral, nasal, conjunctival or vaginal exposure to infective material.^{7,24} Aborting bitches discharge large numbers of infective organisms. The infected male can transmit brucellosis to bitches at coitus for many months by infective semen.²⁴ Organisms from the epididymis, testes and prostate are discharged intermittently in semen. The male dog might rarely spread infection in his urine.^{8,24} Spread of infection by fecal

contamination does not readily occur. When like-sexed infected and uninfected dogs were housed together transmission did not occur.²⁴

The practice of breeding popular stud dogs to large number of females from a wide geographic area or the use of artificial insemination or frozen semen could disseminate the disease widely if the stud should be infected. The aborting female can readily spread **Br. canis** throughout a kennel by contamination of food, runs, and water from aborted fetuses and membranes, genital discharges and even by her milk. Because of the prolonged bacteremia blood transfusions or even the use of contaminated syringes and needles could spread the disease.

Since dogs are the only known natural host for **Br. canis**, transmission to man probably comes from this canine source. Humans appear relatively resistant to **Br. canis** infection unless massively exposed.^{7,9c} Signs in humans vary but resemble those of undulant fever due to **Br. abortus** including intermittent fever, chills, malaise, muscle and joint pain and enlarged lymph nodes. In the U. S. seroprevalence rates in humans was 0.4 percent. Human infections have responded to treatments with tetracyclines. There have been only 18 cases of human brucellosis due to **Br. canis** reported and no known deaths.^{7,24}

Following canine exposure to **Br. canis** a bacteremia develops within 1 to 3 weeks. A generalized lymphadenitis and splenitis occurs and antibodies become detectable by the serum agglutination test. The brucella organisms persist for many months or indefinitely in many organs of the body. After one year blood cultures may become negative in some dogs but a few dogs may have a bacteremia lasting for 26 to 33 months or more. Since clinical signs other than abortion and epididymitis are not specific, a definitive diagnosis is based on serologic and bacteriologic tests, especially the latter.^{7,24}

The organisms can readily be cultured from organs of

aborted fetuses, placental tissues and vaginal discharges. Blood cultures are often positive. Current available serologic screening tests for canine brucellosis must be performed carefully and interpreted cautiously. The slide agglutination test and tube agglutination tests are widely used. The agar gel immunodiffusion test shows promise and is presently being evaluated.²⁴ The slide agglutination test is commonly performed by mixing patient serum with a rose bengal-stained heat-killed *Br. ovis* suspension. Clumping or agglutination is interpreted as suspicious of *Br. canis* infection. However 50 to 60 percent of positive test results are erroneous or false positives. While a negative test is highly reliable, false negatives are rare. Thus a positive test result **must** be confirmed by culture of the organism. The addition of mercaptoethanol to the serum will eliminate about 90 percent of the false positive results.⁶ A recommendation to destroy, castrate or spay serotest positive dogs requires the recovery of the organism by culture procedures. The false positive test results are due to cross reactions to a number of ubiquitous canine organisms. The tube agglutination test is the most widely used serologic procedure to detect *Br. canis* antibodies. The serotiters reported based on this test must be interpreted by the laboratory performing the test but usually a titer of 1:200 is considered positive. However some chronically infected male dogs may be negative by serologic testing. It is interesting to note that even though dogs have positive serologic tests indicating the presence of antibodies in the blood that these dogs may concurrently have a *Brucella* bacteremia. Antibiotic therapy for several weeks will result in a period of abacteremia and false negative serologic test results. After therapy is discontinued the bacteremia will usually recur. A single negative blood culture does not completely indicate freedom from the disease so, especially in treated male dogs, repeated blood cultures might be indicated. Since present serologic tests may not be reliable, a recommendation to destroy, castrate or spay a serotest positive dog should not be made without blood culture.^{6,7,24}

Efforts to develop an effective safe bacterin or MLV vaccine have been unsuccessful and probably is not indicated or desirable.^{6,7} Although *Br. canis* is susceptible *in vitro* to a combination of tetracyclines, dihydrostreptomycin, minocycline, rifamycin; sulfonamides or combinations of antibiotics administered to infected dogs for a number of weeks,^{15b,24,32} therapy has been unsatisfactory as only a one to three-month temporary cessation of the bacteremia resulted. A few antibiotic regimens especially if given early in the disease have apparently resulted in a cure of the disease in certain bitches.³² Such treatment was long term, very expensive and required

repeated confirmatory cultures over many months even after therapy was discontinued.^{6,7,24} Bitches naturally infected with *Br. canis* were treated sequentially for a period of 14 days each with tetracycline 20 mg/kg orally TID, dihydrostreptomycin 11 mg/kg IM, BID and trimethoprim-sulfadiazine 15 mg/kg orally BID. These bitches became abacteremic after treatment and abortions did not occur while they were bacteremic.^{15b}

Prevention and control in kennels is based on eradication by repeated monthly serologic and cultural tests of all dogs, young, old, male and female, segregation and destruction of infected animals, and concomitant sanitary measures. All dogs to be introduced into kennels should be isolated for 3 to 4 weeks and blood tested. Domestic livestock have been shown to be highly resistant to infection with *Br. canis*. There is no evidence that *Br. canis* on inoculation into cattle will cause seroconversion on tests for either *Br. canis* or *Br. abortus*. Cats are resistant to natural infections with *Brucella* spp.^{8,21,24}

Miscellaneous bacterial causes of canine and feline abortion include:

Brucella abortus,¹ *suis*¹⁹ and *melitensis*^{4,7} can cause occasional sporadic abortions in pregnant bitches when they ingest infected material. These cases may be diagnosed on culture of aborted, infected fetuses or membranes and by the serum agglutination test.^{17,22b} As with *Br. canis*, dogs infected with these other species of *Brucella* may transmit infections to humans. Nonspecific organisms such as *coliforms*, *staphylococci*, *streptococci* and *Salmonella* spp. are frequently associated with sporadic abortions especially in older bitches and often accompanied by chronic endometritis and low grade cystic endometrial hyperplasia.^{2,18,20,21,23} These abortions are usually associated with infertility, a persistent vulvar discharge, chronic metritis, and repeated abortions. Few bacteriological studies have been reported in dogs to indicate the incidence of the more common or even the occasional bacterial causes of abortion.

By the administration of large doses of penicillin and streptomycin or other antibiotics for 7 to 14 days or longer, some veterinarians have reported apparent success in preventing abortion in dogs showing early symptoms of impending abortion. Bitches with a history of repeated abortions may carry the conceptus to term if infection was controlled or prevented by treating with broad range antibiotics for several weeks before and after service. Although a few reports have linked *Leptospira pomona* with abortion in dogs, evidence indicates that they do not abort from this cause. Dogs can become urinary shedders of *leptospira*.⁴ *Salmonella* spp. has been re-

ported as a cause of occasional canine abortion and stillbirths associated with the acute disease.²³

Viral causes of abortion—In contrast to the large species of domestic animals, dogs relatively seldom abort due to viral infections of the fetuses. Abortions in dogs have been described following an acute attack of distemper. Viral agents including distemper,^{10,16,18} canine adenovirus¹⁸ (infectious hepatitis) and canine herpesvirus (CHV)^{14,18} have been isolated from aborted fetuses, placentas and neonates. Transplacental transmission of CHV to fetuses may occur late in gestation.^{14b} There is evidence that the latter two viruses may occasionally cause abortion. Canine distemper virus (CDV) can cause transplacental infections and abortion and if late in gestation may cause congenital infections in the newborn pups.^{18a} Vaccines are available for the prevention of disease caused by distemper and infectious hepatitis and should be given before breeding. Canine distemper virus (CDV) MLV or avirulent vaccines should not be administered to pregnant bitches.

Fungal causes of abortion have not been reported in dogs.

Protozoal causes of abortion in dogs are uncommon. *Toxoplasma gondii* may cause abortions, birth of premature, dead or moribund pups or living pups with congenital toxoplasmosis.^{4,8,28} Toxoplasmosis may clinically resemble other infectious diseases of dogs. As with sheep the organism may be recovered from fetal organs and placenta, especially the brain or be observed in histologic sections. The Sabin-Feldman dye test and the complement-fixation test and others are useful serologic tests for toxoplasmosis.^{4,11}

Noninfectious Causes for Canine Abortion

A number of drugs have been described that when administered to pregnant bitches caused fetal death and abortion. These drugs include: N-deacetylthiocolchicine; O-diazoacetyl-L-serine (azoserine); malucidin; a yeast extract and other nonhormonal compounds.^{12,13,27,30,31} These drugs have been suggested for mismatings but have not been generally accepted for this purpose nor proven acceptable for causing abortion in bitches.

Because the dog is highly susceptible to estrogen toxicity by bone marrow depression, thrombocytopenia and leukopenia, large or repeated doses of estrogens to produce abortion has not been attempted nor recommended. Small doses of 0.02 to 0.03 mg/kg of prostaglandin F_{2a} given 2 or 3 times per day between 33 and 53 days of gestation resulted in abortion in 4 or 7 bitches at 56 to 80 hours after treatment was started.^{9b} In some bitches not all the fetuses were expelled. Also undesirable side

effects of salivation, vomition and diarrhea occurred after the injections. A single effective dose of 1 mg/kg is too near the fatal dose of 5 mg/kg to administer. Presently 0.05 to 0.075 mg/kg is given twice a day up to 5 to 7 days to be certain all fetuses are expelled.^{9a} In preliminary studies 2 bitches pregnant 30 days and 2 pregnant 45 days were given 5 mg dexamethasone twice daily for 10 days. In the former the embryos died and were resorbed and in the latter dead fetuses were aborted one and 3 days after the end of the treatment.^{1a} Further studies are indicated. Thus in the bitch there is no satisfactory product or drug to induce abortion even in early pregnancy. The use of dexamethasone to induce abortion or cause premature births in bitches has not been adequately evaluated. Possibly the combination of dexamethasone and prostaglandin might be satisfactory but further trials are indicated. However surgical removal of the corpora lutea in the bitch will result in abortion at any stage of gestation and presently it is the only safe method for termination of pregnancy.⁵

Progesterone deficiency—Abortion in bitches with no evidence of infection may be due to hypoluteinization and occur the sixth to seventh week of gestation because of premature regression of the corpus luteum, or occur the second to fifth week of gestation due to faulty development of the corpus luteum. Five to 25 mg doses of progesterone in oil 2 to 3 times a week until the eighth week of pregnancy, or the "repositol" form could be used less often.² More work needs to be done to assess the incidence of abortions due to endocrine deficiencies.

Nutritional causes of abortion in dogs have rarely been reported. Manganese deficient bitches either failed to come into estrus or when bred, terminated gestation about three weeks later.²⁶ It is rather significant that in our motorized society that only a few abortions in dogs following severe trauma have been described. Genetic defects of the developing embryo or fetus may result in embryonic or fetal death. In bitches, as in sows, the number of developing embryos maturing to term is regulated by uterine factors and spacing of embryos. Most deaths due to these factors occur about 30 days of gestation and embryos dying at this time are usually autolysed and absorbed. Dystocia due to achondroplasia in certain breeds of dogs and lack of proper growth in young animals may cause dystocia and stillbirths.

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Abortion in Queens

Abortion in queens is probably more common than in bitches¹³ but much lower than in sows, ewes, cows and mares. The true incidence is not known because of early embryonic deaths and resorption of the conceptuses and the nature of carnivores to consume aborted material or fetuses. Most feline abortions are sporadic. An increasing number of studies have been performed on the causes of abortion in queens.

Infectious Causes of Feline Abortions

Bacterial Causes

Nonspecific organisms including coliforms (**E. coli**), **Pseudomonas spp.** **Staphylococci**, **Streptococci** and **Salmonella** are associated with sporadic or repeated abortions, early embryonic deaths, mummified and still-born fetuses, in middle-aged or older queens that, as in bitches, may be associated with chronic endometritis and low-grade cystic endometrial hyperplasia. Most of these

Table 13b. Summary of the Causes of Feline Abortions

Infectious Causes

Bacterial causes—none.

Miscellaneous bacterial causes—coliforms, pseudomonas, staphylococci, streptococci and salmonella.

Viral causes—feline panleucopenia virus, feline herpesvirus (feline viral rhinotracheitis), feline leukemia virus (?).

Other infectious causes—mycoplasma, *Toxoplasma gondii***Noninfectious Causes**

Hormonal causes—progesterone deficiency (?), prostaglandins.

Physical causes—severe trauma (?)

Miscellaneous causes—genetic defects, parturient conditions and stillbirths.

abortions are observed after 4 to 5 weeks of gestation with an apparent greater incidence in short-haired queens.^{3,13,14,19,20} These reproductive failures are often accompanied by a prolonged discharge from the genital tract and a history of infertility. Although of questionable value, prompt administration of broad-range antibiotics may prevent abortion in queens exhibiting signs of impending abortion. Culture of the discharge and sensitivity testing might improve the results of treatment. Those with a history of repeated abortions might benefit from antibiotics given for several weeks before and after breeding. This above syndrome, not uncommon in queens, may be associated with immunosuppressive viruses such as the feline leukemia and possibly feline infectious peritonitis viruses¹⁴ as well as the abnormal uterine changes in older queens due to chronic hormonal stimulation associated with estrous cycling and pseudo-pregnancy and the steroid hormones, progesterone and estrogen.¹⁵

Cats are resistant to natural infection with *Brucella* spp.¹⁵ Although when infected they can become urinary shedders of *Leptospira* spp., abortions do not occur.^{1,6}

Viral Causes

Feline panleucopenia (FPL) virus, a parvovirus, causes embryo resorption, mummified fetuses, abortions, stillbirths and cerebellar hypoplasia or aplasia in neonates infected late in gestation.^{2,3,5,9,12,14} Signs of ataxia associated with cerebellar dysplasia is often not noted until the kitten is 2 to 3 weeks old. As in parvovirus infection in swine not all fetuses in a litter may become infected.

Feline panleucopenia, feline infectious enteritis, or "distemper" is a highly contagious viral infection seen world-wide in all breeds of cats. It is characterized by a marked leucopenia, fever, depression, anorexia, vomiting and a profuse diarrhea especially seen in young susceptible kittens after 2 or 3 months of age when they have lost their colostral immunity. Acutely infected animals shed virus in all body excretions and for up to one year in the urine. It is easily spread by indirect contact as the virus is very stable.

The virus may be recovered by viral isolation from aborted fetuses or demonstrated by immunofluorescence of infected tissues. The serum-neutralization test is used to detect antibody which rises rapidly to reach a high level about 10 days after the onset of illness.^{2,5,9}

The disease may be prevented by vaccination with an inactivated or MLV vaccine or combined FPL and FVR vaccines available commercially. The latter MLV vaccines should not be used in pregnant queens. After the initial series of vaccinations as kittens, once a year revaccination is recommended for maximum protection. Treatment of exposed pregnant and possibly susceptible queens should be with antiserum or normal feline serum at a rate of 1 ml/lb. to provide immediate protection.^{9,14}

Feline viral rhinotracheitis (FVR) or feline herpesvirus 1 is wide-spread and causes an upper respiratory disease that varies from a subclinical condition to marked respiratory signs and death. It is characterized by sudden onset, pyrexia, leucocytosis, sneezing, coughing, nasal and conjunctival exudate, and anorexia.^{2,3,5,12,14} Occasionally secondary bacterial pneumonia, dendritic keratitis, and vulvo-vaginitis may occur. If pregnant susceptible cats become infected about the sixth week of gestation, mummified fetuses, abortion, stillborn or congenitally infected, weak newborn may result as this feline herpesvirus crosses the placental barrier. As with other herpesviruses a carrier or latent infection in the trigeminal ganglion often results with recrudescence spontaneously or at periods of stress such as parturition.^{7,8} Carriers or acutely infected cats transmit this infection by the respiratory route. This feline herpesvirus 1 is distinct from the herpesvirus virus described as the possible cause of feline urolithiasis.⁹ Other agents such as feline calici (picorna) virus, feline chlamydial infection (pneumonitis), reovirus, and Bordetella and Pasteurella also cause respiratory disease in cats that may resemble feline viral rhinotracheitis. Diagnosis of FVR infection can be made by viral isolation from fetuses or placentae, by the fluorescent antibody test or by finding intranuclear inclusion bodies typically seen in herpes virus infected tissues on histopathological examination. Inactivated and

MLV vaccines for intramuscular use and an MLV vaccine for intranasal and conjunctival administration are commercially available. The MLV vaccines should not be used in pregnant queens. Presently commercial vaccines combining the feline viral rhinotracheitis and panleukopenia viruses are also available.

Other feline viruses such as the calici (picorna), feline infectious peritonitis (FIP), reovirus and chlamydial organisms have not been reported to cause abortion in cats.⁹

In the mid to late 1970's a wide-spread syndrome occurred in a near epizootic manner in many catteries and breeding colonies in the U.S. This kitten mortality complex (KMC) was an apparently new disease characterized by a high incidence of reproductive failures and kitten deaths including: repeat breedings and failure of conception, abortions the last trimester of pregnancy, stillbirths, congenital malformations, endometritis and pyometra with a bloody vulvar discharge, chronic upper respiratory disease and conjunctivitis, intermittent pyrexia, acute cardiovascular disease and kittens dying within a few days or weeks of birth.^{16b,18c} Careful studies failed to reveal any bacterial or viral etiologic agent. However, nearly all affected cats were serologically positive for feline infectious peritonitis (FIP). In recent years the incidence of this KMC syndrome has greatly declined.

Feline leukemia virus (FeLV) is probably world-wide in distribution and causes a number of clinicopathological syndromes including alimentary, thymic and multicentric lymphomas, leukemia, anemia, panleukopenia-like syndrome, enlarged kidneys, thymic atrophy and other FeLV immunosuppressive diseases. The FeLV virus may be transmitted horizontally, especially in young kittens, or vertically from viremic queens. More often, however, early embryonic deaths and resorptions or abortions have been reported.^{3,9,10,11,14} Thus even if feline leukemia virus doesn't actually cause abortion or resorptions it may favor disease processes that produce them. Further studies are needed to delineate the exact role of FeLV in reproductive losses.

Unless obvious disease states such as tumors are present, a diagnosis of feline leukemia-sarcoma complex requires laboratory assistance.⁹ Blood examinations, histopathological, serological and virological procedure may all be used. The most common simple rapid tests are the immunofluorescent antibody (IFA) test applied to blood smears¹¹ and the commercially-produced ELISA test that can be performed in the veterinary hospital, which detect the FeLV or antigen in the blood. This latter test is more sensitive and may detect transiently infected cats so a second test about a month later is indicated to determine the chronically FeLV infected cat.^{18b} The FOCMA (feline oncovirus-associated cell membrane antigen) test for

the presence of antibody can help assess the resistance of a cat. On the basis of these and other tests the prognosis in a given case may be determined.⁹

Although work has been undertaken on the development of a FeLV vaccine, none is presently available. The greatest numbers or incidence of FeLV-infected cats have been found in large breeding catteries; while a much lower percentage of positive cats have been found in one or two cat households or in free-roaming cats. An IFA or ELISA test positive cat is carrying the FeLV virus whether it appears healthy or diseased and is probably shedding the virus.^{9,11} By using the above tests FeLV-free colonies can be established and maintained by not allowing infected cats into the disease-free colony. This is essential for a breeding cattery.

Mycoplasmosis due to *M. gateae* has been described as a cause of feline abortions at various stages of gestation.²²

Fungal causes of abortion in cats has not been reported.

Parasitic Protozoal Causes—Toxoplasmosis due to *Toxoplasma gondii* was formerly reported in queens as the occasional cause of embryonic resorptions, fetal mummification, abortion and death of neonates, possibly due to transplacental infections.^{1,14,17,21} A more recent well-controlled study indicated that *T. gondii* is not likely to be an important cause of abortion or perinatal mortality in cats and transplacental transmission could not be demonstrated.^{3,4a,b} However cats can harbor and excrete oocysts from their intestinal tract of four coccidial parasites, *Toxoplasma*, *Hammondia*, *Sarcocystis* and *Besnoitia*.²³ Toxoplasmosis in kittens or older cats can easily be clinically confused with other feline diseases.^{4b}

Noninfectious Causes for Feline Abortion

Recurrent abortions in queens might be due to a **progesterone deficiency** when other causes cannot be determined.^{1a} These abortions usually occur from the second to seventh week of gestation. It was suggested that 5 to 25 mg doses of progesterone in oil be administered two to three times a week until the eighth week of gestation or the repositol form could be used once or twice a week. Further studies might be informative if a number of queens with habitual abortions could be examined throughout pregnancy by hormonal assays.

Prostaglandin F_{2α} at doses of 0.5 to 1.0 mg/kg once or, if necessary, twice at 24 hour intervals caused abortions in all pregnant cats over 40 days of gestation within 24 or 48 hours, respectively. Queens pregnant 55 days

or longer gave birth to live kittens, lactated normally and suckled their newborn.¹⁶ This treatment in contrast to bitches given prostaglandin, was well tolerated. Another preliminary study²⁴ indicated that PGF_{2α} alone did not cause abortion in queens in late pregnancy unless combined with ACTH. Prostaglandin did not induce abortions when administered prior to 40 days of gestation.^{18a}

Estradiol cypionate (ECP) in a single dose of 0.25 mg given intramuscularly will prevent conception if given within 1 to 5 days, preferably about 40 hours after coitus, if the time of coitus is known.¹⁴ This treatment apparently retards the passage or locks the fertilized ova in the uterine tubes where they degenerate. Signs of estrus may be prolonged. Repeated estrogenic therapy should be avoided in queens, although they are not as susceptible to estrogen toxicity with bone marrow depression and thrombocytopenia as the bitch.^{18a}

Nutritional causes of abortion in queens have not been reported. Some feline abortions have been associated with severe anemia or pregnancy toxemia.¹³ As in other species genetic or chromosomal defects can cause early embryonic deaths, abortions or defective weak neonates.

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Abortion in the Queen

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Mummification of the Fetus

Fetal death in domestic animals occurring the middle or last third of gestation that does not result in involution of the corpus luteum and abortion of the fetus within the next week or 10 days or decomposition or maceration of the fetus within the next several months, is followed by autolytic changes in the fetus, absorption of placental and fetal fluids, involution of the maternal placenta, and mummification of the fetus. Conditions necessary for the occurrence of fetal mummification include the maintenance of the dead fetus within the uterus by the presence of a normal viable fetus or fetuses or the persistence of the corpus luteum of pregnancy associated with a single, or rarely twin, bovine mummified fetuses. One or more mummified fetuses present in the uterus with one or more



Figure 71. Mummification of twin, bovine, 3-month-old fetuses. These were spontaneously aborted at four months of gestation.

normal viable fetuses is observed frequently in sows, occasionally in bitches and queens and uncommonly in ewes, does, cows and mares. Fetal mummification associated with a persistent corpus luteum is observed in the cow, doe, sow and bitch. The maintenance of pregnancy in these species is due to progesterone produced by the corpus luteum. In the other species progesterone is produced by the fetal placenta or chorion after midgestation and the corpora lutea involute. Fetal mummification apparently does not occur the first trimester of gestation because embryonic or fetal death prior to the development of the fetal bones usually is followed by resorption of the fetal and placental tissues. Fetal death the last month or six weeks of gestation with beginning fetal mumi-



Figure 72. Removal by cesarean section of a bovine mummified fetus that died at 7 months of age.

fication may be undiagnosed at parturition and called a stillbirth, especially in multiparous animals. Williams¹⁹ described some of these fetuses in cows as "static fetal cadavers." Fetal mummification may occur and subsequently bacteria may invade or gain entrance to the uterus and cause secondary maceration of the uterine contents.

Two types of fetal mummification have been described in animals, the hematic type in cattle and the papyraceous type in all the other species. The process by which these two types form are basically similar. In cows as the maternal placenta or caruncle undergoes involution a variable amount of hemorrhage occurs between the endometrium and fetal membranes which after the plasma has been absorbed leaves a reddish-brown, gummy, tenacious mass of autolyzed red cells, clots and mucus. This imparts a reddish-brown color to the fetal membranes and fetus. A similar discharge of blood from the caruncles is noted in normal parturient cows 10 to 14 days after calving and is characterized by a bloody genital discharge. The similarity between the tenacious sticky reddish mucus around the membranes of the bovine mummified fetus and that found in the rectum following intussusception of the intestine in cattle is strik-

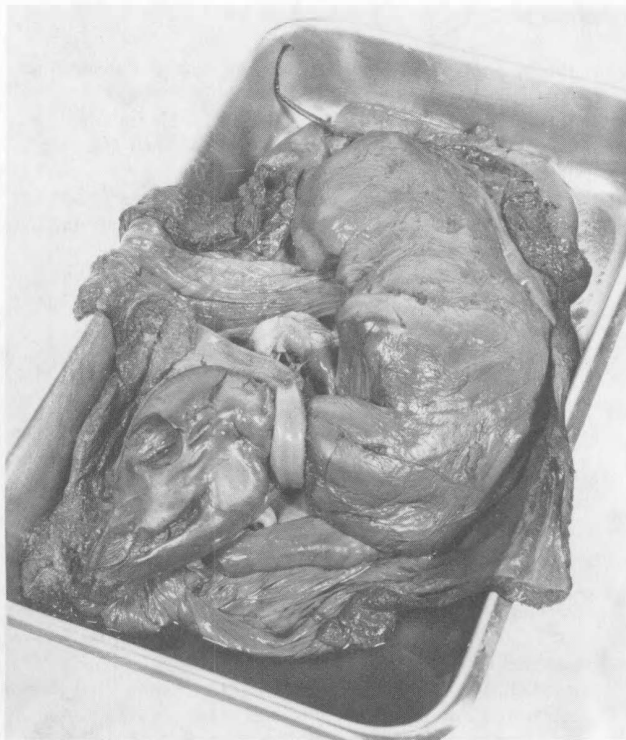


Figure 73. Death and mummification of a bovine fetus due to the displacement of the umbilical cord around the neck of the fetus.

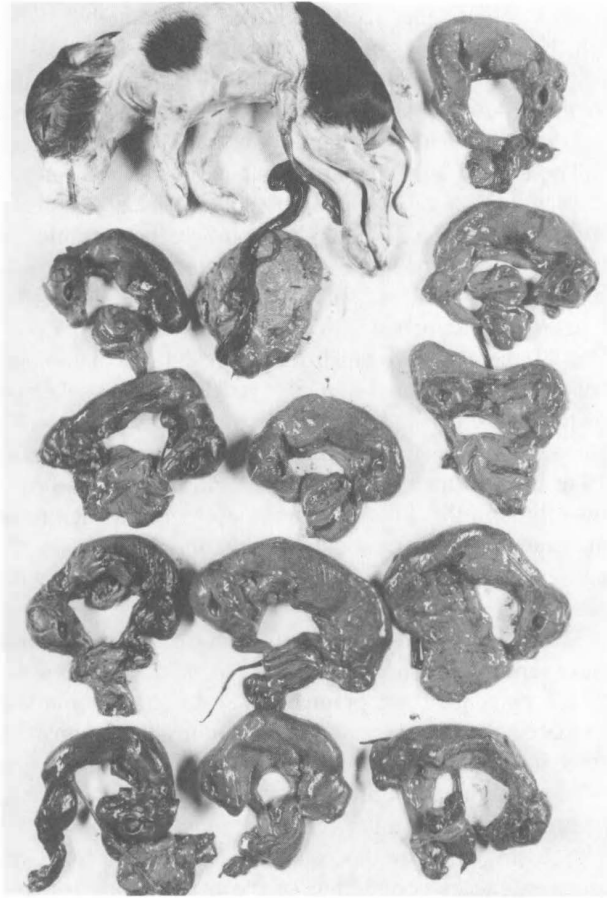


Figure 74. Porcine fetal death and mummification at different times in gestation and a stillbirth, with abortion of the uterine contents near term. This might possibly have been due to a parvo-, entero-, or pseudorabies virus.

ing. In the other species mummification is not characterized by placental hemorrhage and the fetus is usually a brownish color and the fetal membranes are not covered with this reddish-brown tenacious material. In both types of mummification the longer the condition exists the greater the loss of fluids from the placenta, the membranes and the fetus.

Mummification of the bovine fetus is observed most often in Guernsey cattle although other breeds are commonly affected. The condition usually affects single fetuses but may occasionally involve one or both fetuses in twin pregnancies. Bovine fetal mummification occurs during the third to eighth month of gestation but most commonly the fourth, fifth and sixth months (See Figures 71, 72, 73). If the condition is undiagnosed the mummified fetus may remain in the uterus for months beyond a normal gestation period. Spontaneous abor-

tions before, near, or after the expected end of gestation are not uncommon. In one study of 32 mummified fetuses in one herd the range of the "gestation," period from conception to spontaneous abortion, was 131 to 342 days with an average of 215 days.⁵ The sex of mummified fetuses are nearly equally divided between males and females.¹¹ No premonitory signs are observed before the expulsion of a mummified fetus except occasionally those of estrus.

The causes of fetal death and mummification in cattle are often the same as causes for fetal death and abortion. The cause of fetal mummification is often impossible to determine because the time of death is not known and autolysis and mummification of the fetus and membranes makes isolation and determination of the causative agent difficult or impossible. Serologic tests of the dam weeks or months after fetal death are usually of little diagnostic significance. Fluorescent antibody staining of tissues have been helpful in some cases.

Genetic factors may be involved in bovine fetal mummification.¹¹ There is a greater incidence in the Guernsey and Jersey breeds of cattle. Certain cow families will have mummified fetuses in two to four generations of cows bred to apparently unrelated males by artificial insemination. In these and other studies the male did not seem to play a causative role in the genetic inheritance of this condition. However, one report¹⁶ suggested that abortions and fetal mummification experienced in a Holstein herd at 120 to 180 days of gestation when daughters of two popular sires were mated artificially to the other sire were due to autosomal recessive genes. In another large Holstein herd⁵ the heritability of fetal mummification was only 16 percent when the service sire was excluded and the condition was not transmitted as a simple recessive. When the owner used other bulls on these cows the losses stopped. Further evidence that this condition may be due to an inherited endocrine or other defect of certain cows is the fact that as many as 20 to 50 percent, average 30 percent, of subsequent conceptions in cows that have had mummified fetuses may result in fetal mummification whether the same or different sires were used.¹¹ The author observed one Guernsey cow that had 5 normal calves and 5 mummified calves within a period of 9 years. In such cows abortions at midgestation not associated with fetal mummification are quite common. The possibility of a latent virus or organism residing in the uterine or other body tissue or cells and causing the repeated occurrence of mummified fetuses in the same individual should possibly be considered although evidence for this has not been reported. Rare cases of mummified anomalous calves are recorded.

Other causes for bovine fetal mummification include

torsion of the umbilical cord or compression of the umbilical cord by its passing around a fetal extremity (See Figures 66 and 73). This causes fetal death. Fetal mummification may then occur instead of prompt abortion. There is evidence that fetal mummification may follow infectious causes of fetal death such as *C. fetus*, molds, leptospirosis, IBR and BVD-MD virus.^{8,9a,11} Leptospirosis and BVD-MD virus may account for the occasional epizootic outbreaks of fetal mummification in a herd. Fetal death and a degree of mummification may occur in animals in which the duration of gestation has been prolonged by progesterone or progesterone-like compounds. Torsion of the uterus and trauma are not considered to be causes of fetal mummification. Wound infection organisms causing an inflammatory response in the endometrium with possible release of prostaglandins are characterized by fetal death and prompt abortion and not by fetal mummification. Almost all mummified fetuses and uteri when examined and cultured are sterile and free of organisms and the endometrium is involuted and no inflammatory lesions are present. This is further substantiated by the observations that cows usually conceive the first or second estrum after the expulsion of the mummified fetus. The causes of fetal mummification in the other species should be noted as these might provide leads for explaining the causes of the condition in cattle.

As the fetus mummifies and fetal and placental fluids disappear, the uterine walls contract and tightly enclose the conceptus. The longer the condition exists, the dryer, firmer, and more leather-like the tissues of the fetus become. In the cow the uterine walls are fairly thick and no cotyledons are palpable. The uterine artery is small and has no fremitus. Fetal mummification in the cow is characterized by failure of estrum with a persistent corpus luteum. It is usually not suspected until late in gestation or until after the normal length of gestation, when normal development of the fetus, body and udder changes incident to parturition and calving fail to occur. Although the uterus may be drawn forward by the weight of the mummified fetus and a normal cervical seal may be present, a careful rectal examination will readily reveal the nature of the disease. If the uterus is dropped downward out of reach it may be pulled up to the pelvic cavity manually by grasping the cervix or intercornual ligament, by placing Knowles cervical forceps on the cervix and drawing the uterus back, or by having two men raise the caudal abdominal viscera by means of a pipe or bar held by each of them. Rarely a large mummified fetus may be ballotted through the flank. In cases where the uterus is examined very early after the death of the fetus and the occurrence of the interplacental hem-

orrhage, the former feels distended by a doughy mass, which is the large, soft blood clot. The fetus is not easily palpated in this doughy mass within the contracting uterus. Within a few weeks the typical changes associated with fetal mummification in the cow become apparent.

The bovine fetal mummy remains in this semi-moist state without odor or pus until spontaneous abortion results in from 1 to 2 months to 1 to 2 years, or until the condition is diagnosed, treated, and corrected, or the animal is slaughtered. If spontaneous abortion occurs, the fetus may be expelled into the vaginal cavity and a portion of the dark brownish-red stained fetal membrane hangs from the vulva until noticed by the caretaker or owner. Estrum usually occurs about the time of the spontaneous abortion and the cow will come into estrum again 16 to 24 days later. If the fetus should be large and passage through the dilated cervix is not possible then fetal maceration may occasionally result. In large fetuses tenesmus or straining, as noted in other abortions, may be observed.

The incidence of fetal mummification in cattle is low and sporadic. In three large herds the incidence was 0.43 to 1.8 percent of the pregnancies.¹¹ In some herds the incidence may be higher and in a few instances apparent epizootics of mummified fetuses may occur.

To expel the mummified fetus in the cow the simplest treatment is to administer 50 to 80 mgs. of stilbestrol or 5 to 10 mg. of estradiol intramuscularly. The injected estrogen causes contraction of the uterine muscles, relaxation of the cervix, involution of the corpus luteum and results in the expulsion of the fetus. In about 80 percent or more of the cases this single injection of an estrogen is all that is required and the fetus is expelled within 37 to 72 hours. If the fetus has not been expelled within this time, a similar dose of estrogen may be administered a second time. In unusual instances 3 or more doses at 48-hour intervals may be needed. Some veterinarians use repositol diethylstilbestrol, 100 to 150 mg., intramuscularly. In one study of 50 cows with mummified fetuses, daily injections of estrogens were given and all expelled the fetuses in 3 to 11 days.¹⁷ Occasionally examination of a cow either after treatment or before will reveal the fetus entering into or wedged in the cervical canal, with the cervix not yet dilated sufficiently to allow passage. Administration of a single large dose of estrogen at this time usually results in successful dilation of the cervix and the expulsion of the fetus within 24 to 36 hours. When the fetus is large, or mummification occurs at 6 to 8 months of gestation, or the cow is small or immature, the genital tract should always be examined within 48 to 72 hours after the injection to make certain failure of expulsion or dystocia does not occur

with secondary infection of the uterus, closure of the cervix and maceration of the fetus. Occasionally a second dose of estrogen, much lubrication, gradual traction with a snare or Knowles cervical forceps by one hand and pushing on the fetus with the other hand in the rectum, may be needed to help remove the fetus.

In recent years a number of reports have indicated that the injection of prostaglandin or its analogues in luteolytic or somewhat larger doses intramuscularly such as 25 to 50 mg of prostaglandin $F_{2\alpha}$ or 500 ug cloprostenol (**Estrumate**), caused the involution of the corpus luteum and the expulsion of the mummified fetus 72 to 120 hours later.^{7,17,18} Plasma progesterone levels dropped rapidly from about 10 ug/ml to 1 ug/ml and estradiol levels were low about 3 pg/ml during the postinjection sampling period. However in most reported cases it was necessary to withdraw the fetus from the cervix and cranial vagina by traction due to the incomplete relaxation and dilation of the vagina and vulva. Possibly the combination of estrogens and prostaglandin would be more effective in producing expulsion of the mummified fetus and relaxation of the genital tract. Further studies are indicated as in some cases after prostaglandin therapy and rare cases after estrogen therapy the corpus luteum would involute but the mummified fetus would not be expelled.^{11,17} Glucocorticoid treatment of cows with mummified fetuses failed to induce luteolysis and expulsion of the mummy. A live fetus is necessary for dexamethasone to effect abortion or premature delivery.^{1,1b,17}

Removal of the persistent bovine corpus luteum of pregnancy will usually result in estrum and evacuation of the uterus. There is the added danger of trauma and damage to the ovary by the forceful or surgical removal of the deeply imbedded corpus luteum of pregnancy. It has been found that massage of the uterus daily for several days frequently provides enough stimulus to cause evacuation of the uterus. Manual dilation of the cervix is not indicated. It has been reported that filling and distending the vagina with cotton will cause the expulsion of a mummified fetus. The author has had no experience with this method of treatment. It is possible that manual uterine massage or distention of the vagina stimulate the release of oxytocin and prostaglandin to effect expulsion. In exceptional cases in which the affected animal is a small heifer, or the fetal cadaver is very large or previous treatment has been unsuccessful, a cesarean operation through either the right or left flank is usually successful in correcting the condition.

Following treatment and expulsion of the mummified fetus, most cattle recover promptly since no infection is present to delay recovery. Conception usually occurs

within 1 to 3 months. Any cow with a history of having one mummified calf may abort at 3 to 8 months of gestation or have another one at any gestation period; hence the prognosis should always be guarded.

Fetal mummification in horses occurs seldom and has only been reported in one of twin fetuses that has died during pregnancy probably due to a lack of placental area. The equine mummified fetus remains in the uterus only as long as pregnancy is maintained by the viable twin.¹² Since spontaneous abortion of twin fetuses is common in mares the discrepancy between the size and development of the partially mummified fetus and recently dead fetus often leads to the improper diagnosis of superfetation. Mummification of both fetuses in a twin pregnancy has not been reported in the mare.

Fetal mummification in sheep is occasionally observed as affecting single ovine fetuses or one or both twin fetuses. It has been associated with and probably caused by infections in sheep causing fetal deaths and abortions. These include: toxoplasmosis, EAE (Enzootic abortion of ewes or Chlamydiosis), **Listeria monocytogenes**, possibly **L. pomona** and unknown causes associated with prolonged gestation.¹¹

In does, as in ewes, fetal mummification is uncommon but it has occurred affecting one of twin fetuses in chlamydiosis, in toxoplasmosis, in Border Disease (BVD) and possibly in Coxiella infection.^{13,14,15} Two rare cases were reported in does. One was a case of twin hybrid mummified fetuses resulting from a mating of a ram and a doe and the other in a doe that ingested a toxic dose of Japanese pieris.^{13,14}

Fetal mummification in swine is an important cause of prenatal losses. Fetuses dying *in utero* from 40 to 90 days of gestation usually mummify and are expelled at parturition along with the normal fetuses. In a herd relatively free of disease, single mummified fetuses in a litter were more common than two or more.¹⁰ In three breeds of pigs in this herd, Berkshire, Chester White and Yorkshire, the percentages of mummified pigs were 4.97 and 1.95 and 1.08, respectively. The high incidence of mummified fetuses in Berkshires in this herd accounted in part for the smaller litter size in this breed. Single mummified fetuses were more common in large litters. The presence of occasional mummified fetuses were not related to the incidence of stillbirths. The cause of these occasional mummified fetuses in certain litters is not known. Epizootic herd outbreaks of abortions, early embryonic deaths, mummified fetuses and stillbirths have been described in swine (See Figure 74). A high incidence of mummified porcine fetuses has been reported due to the following viruses: Aujeszky's or pseudorabies, Japanese encephalitis B, Japanese hemagglutination, hog

cholera, picorno or entero-viruses,^{3,4} parvovirus, reovirus, cytomegalovirus and possibly swine influenza virus. Fetal mummification also occurs due to leptospirosis in pregnant sows (see abortion in swine). In these viral diseases mummification, when it affected all or nearly all of the fetuses, occasionally resulted in a prolonged gestation period.^{1,3} Following outbreaks of the above viral diseases, affected sows usually conceive promptly and produce normal litters. A natural immunity is apparently produced.

Fetal mummification in dogs and cats is uncommon and sporadic in nature but apparently similar to that seen commonly in swine where one to three mummified fetuses are expelled with normal neonates at the time of parturition. Occasionally in the bitch and more often in the queen the uterus may rupture in late gestation due to torsion or trauma and some fetuses escape into the abdominal cavity and mummify^{1a,9b} (see Extra-uterine Pregnancies and Fetuses).

Fetal Maceration

Maceration may occur at any stage of gestation and has been observed in all species. It is described most often in the cow. (See Figures 75 and 76.) When the fertilized ovum or embryo succumbs to bacterial or viral infection or other disease or abnormality early in gestation it is usually absorbed in the uterus or a slight and often insignificant purulent uterine or vaginal discharge may be evident. The embryo is seldom observed. The interval between estrual periods may be prolonged if the embryo did not succumb until 20 to 50 days after conception. Early embryonic death and maceration are prob-

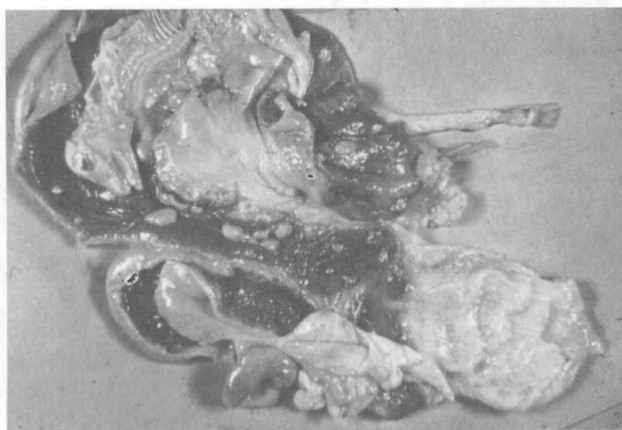


Figure 75. Maceration of a 4-month-old bovine fetus.



Figure 76. Bones of a 6-month-old macerated bovine fetus in the uterus. Note the thickened uterine wall and degenerated fibrotic endometrium (Courtesy K. McEntee).

ably caused by a variety of miscellaneous organisms that may be found in the uterus, and are of common occurrence in cows affected with trichomoniasis or vibriosis. In occasional cases of pyometra seen in trichomoniasis, fetal shreds and placental remnants are often found floating in the purulent exudate. In cases of early fetal maceration the cervix may be tightly sealed or some discharge of pus may be evident in the vagina or from the vulva. These cases usually are diagnosed and treated as pyometra or endometritis. In the former, estrus is not present; in the latter estrus may occur. In multipara, maceration of early embryos and fetuses usually ends in their being absorbed. The other fetuses develop normally or occasionally some become macerated in turn by the extension of the infection. Rarely in cows, ewes, does and mares one fetus may die the first half of gestation and macerate and be expelled with the placenta and the normal twin at parturition.

In the cow fetal maceration that occurs after the third month of gestation, by which time fetal bones are fairly well developed, may be caused by wound-infection type bacterial agents, especially *C. pyogenes*. Septic metritis of pregnancy, resulting in the death, emphysema, and maceration of the fetus in a closed uterus, is uncommon. It may be caused in the cow by the death or mummification of the fetus, followed by a dilation of the cervix and an incomplete abortion and/or dystocia usually occurring from the middle of gestation to near term. The symptoms of septic metritis of pregnancy are similar to septic metritis after parturition. The condition may be more serious or fatal due to the presence of the decomposing fetus(es), failure of the cervix and genital canal to dilate normally, and a uterine inertia.

In rare instances fetal emphysema and maceration may be associated with uterine torsion during gestation. The two factors of an open cervix and a dead fetus at body temperature cause a rapid bacterial invasion of the fetus and membranes of organisms already present in the uterus or from the more caudal portions of the reproductive tract. Fetal emphysema and maceration follow. If the bovine fetus is beyond the third month of pregnancy and if the usual expulsive efforts are not observed or are unsuccessful, the fetus develops emphysema in 24 to 48 hours and in 3 to 4 days maceration begins. If fetal emphysema and maceration develop in a fetus late in gestation, the handling or treatment of the case is the same as similar cases occurring as a sequelae to an ordinary dystocia at or near term and will be described later under the handling of dystocia.

Because of the relatively smaller size of the fetus, those cases of fetal emphysema and maceration accompanying an abortion during the middle period of gestation are treated differently. Usually these cases have a history of intermittent straining for several days accompanied by a foul, fetid, reddish-grey vulvar discharge. The temperature and pulse are often elevated. Anorexia and drop in milk production may be present. Occasionally diarrhea is present. Palpation per vagina or rectum of a distended, swollen fetus with gas crepitating in the tissues is diagnostic of fetal emphysema. In bovine abortion from the fourth to seventh month with fetal emphysema, the fetus usually may be removed by careful and gradual traction if the cervix is sufficiently dilated and much lubrication is used. In the mare the cervix may be carefully dilated manually prior to removal of the decomposing fetus. After removal the uterus should be reexamined to make certain another fetus is not present and to remove the placenta if possible. Aftercare is similar to that described for septic metritis and retained placenta. In those few cases in cattle in which the cervix is contracted and the fetus cannot be removed, heroic treatment is not indicated. Supportive treatment consisting of antibiotics and sulfanomides parenterally along with large doses of estrogens, 50 to 100 mg. of stilbestrol or 5 to 10 mg. of estradiol daily or every other day for perhaps 4 to 7 days, is administered until the cervix is relaxed enough or the fetus is macerated sufficiently to effect its removal in its entirety or in pieces without injury to the cow. With this treatment the danger of excessive traction or fetotomy causing lacerations or rupture of the cervix and uterus is avoided. Because the uterus and its contents are relatively small the development of a septic metritis and a severe toxemia is prevented by the supportive therapy. Cesarean section should be considered as a last resort in the cow, ewe and doe but is seldom required. The ani-

mal should not be rebred for at least three to four months and the outlook for her reproductive life is guarded. Aftercare and treatment of the infected uterus is necessary.

In long-standing cases of fetal maceration the acute emphysematous stage has passed, straining is seldom observed, and the cervix is usually contracted. Generalized symptoms of elevated temperature and pulse and anorexia are not present. There is often a history of a chronic, fetid, mucopurulent discharge from the vulva over a period of several weeks or months. Only rarely is the cervix sealed. There may be a history of a gradual drop in milk flow and a loss of weight. The presence of diarrhea is variable. Diagnosis in the bitch and queen is aided by abdominal palpation, for loss of fluids and crepitation, and radiographs besides observing the other symptoms. Radiographs in the bitch, queen, and possibly the ewe, doe and sow may reveal late fetal death and maceration by the presence of fetal gas and cranial bone overlap. In the bitch dead fetuses curl into a posture resembling the letter C.⁶ In the bitch and queen laparohysterotomy or hysterectomy may successfully correct fetal maceration and the former operation may be followed by conception.² In most cases no external symptoms of illness are noted except possibly a uterine discharge appearing occasionally at the vulva. On rectal examination in the cow or mare, fetal bones may be palpated in the uterus either floating in pus or crepitating against each other with some exudate around them. The uterine wall is thick and heavy and the cervix is usually large and hard. In these cases severe degenerative and sclerotic changes have occurred in the endometrium.

The prognosis is poor. Treatment in the cow is difficult. If much pus is present, treatment as for pyometra is indicated and possibly the bones may be passed through the cervix with the pus. More often the amount of pus is slight and the condition has existed long enough so that the bones are deeply imbedded in the endometrium and uterine wall. The cervix is hard and indurated and not dilatable even with estrogens and prostaglandins. Laparohysterotomy is difficult because of the small size of the uterus and its infected contents. It is seldom indicated and then only as a last resort in a valuable cow, since the future breeding life of these cattle is very questionable. The longer the condition has existed the greater the damage to the endometrium and the poorer the prognosis. In most cases in cattle, slaughter is recommended. In multiparous animals hysterectomy or hysterotomy may be performed, depending upon the circumstances.

In rare instances fetal emphysema and maceration may cause a local perimetritis or even rupture of the uterus, with the macerating fetus being walled off in the abdominal cavity where it may remain indefinitely; or the mass

may slough through the abdominal floor, into the rumen or into the rectum. In rare cases, torsion of the uterus may cause a similar condition in the cow and multipara.

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Fetal Mummification and Maceration

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Prevention of Conception after Mismating and Induced or Artificial Abortion in Domestic Animals

Induced or artificial abortion or preventing of conception is occasionally desirable in veterinary medicine from an economic or therapeutic standpoint. For example if a purebred female is bred by accident to a scrub male or a male of another breed, or if a female is bred at too young an age, induced abortion is often indicated. The earlier this abortion is brought about, the less time is lost in the female's reproductive life and the fewer complications that may arise. Abortions are often desirable in meat-producing animals upon entering the feed lots. If the owner of an animal requests an abortion there are no legal complications to consider as in human medicine. Induced abortion by the administration of hormones has also been discussed under the causes for abortion in each species. Prevention of conception following accidental breeding will now be considered.

The most conservative methods of preventing conception or producing abortion should be used. Heroic measures while often effective may adversely affect the animal's health or its future potential as a breeding animal.

Prevention of conception following an accidental or unwanted service is best accomplished in animals by the injection of an estrogen within 24 to 48 hours after the undesired service. In the cow or heifer 40 to 80 mg. of stilbestrol or 5 to 10 mg. of estradiol intramuscularly usually prevents conception. In the mare this dose should be repeated 48 hours later. In the bitch 0.1 mg/10 lb of body weight up to a maximum of 1.0 mg. of estradiol cypionate (ECP) may be given intramuscularly^{8,9} 9 to 12 days after the onset of proestrus bleeding, 3 to 5 days after the onset of estrus or within 1 to 2 days after a mismating. Rarely toxic or fatal complications due to bone marrow depression may arise even with the modest but effective dose recommended. Estrogens are probably contraindicated in valuable bitches.^{8,9,12} Estrum is usually prolonged 2 to 10 days. In the queen mismating may be treated with 0.25 mg. of estradiol cypionate (ECP) about 40 hours after coitus or from 1 to 5 days after the cessation of estrus. As in the dog this dose may be repeated but excessive doses of estrogens are contraindicated.^{7,9} Conception fails to occur after estrogen therapy due either to the locking or slowing of the passage of the fertilized ovum through the uterine tube,⁷ its too rapid passage through the uterine tube and uterus, or else to the production of an uterine environment inimicable to the development of the early embryo.

The practice of douching female animals with mild antiseptics immediately after service often fails to prevent conception because in the cow, sperm cells reach the pavilion of the oviducts in less than 4-1/2 minutes

and in other species it is apparently only a matter of minutes for some of the spermatozoa to reach the oviducts and hence out of reach of the antiseptic douche fluid. There is no need or reason for a veterinarian to attempt to "separate" copulating dogs even when this is desired by the owners. This is difficult, dangerous and often highly embarrassing. By the time the dogs are separated sperm cells have advanced into the cranial portions of the uterus.

In the bitch, a number of steroidal, usually progestational, compounds have been used to prevent pregnancy in the past, but have proven unsatisfactory because they produced uterine disease.^{3,12} Presently megestrol acetate is satisfactory for use for short periods of time at a dose level of 0.25 mg/lb. daily for 30 days to prevent the development of estrus. It is also administered at a dose level of 1.0 mg/lb. for 8 days beginning during the first 3 days of proestrus bleeding and vulvar swelling to prevent ovulation and corpora lutea formation. This latter treatment usually shortens the interval between estrous periods to 3 to 5 months.^{3,12} **Mibolerone**, a potent orally-active synthetic androgen is now approved for long term estrus prevention in the bitch. Daily administration at a dose rate of 60 to 200 ug daily is required and treatment may be continued for up to two years.^{3,4,12} Side effects are minimal and consist of enlargement of the clitoris, vulvo-vaginitis and occasionally a worsening of seborrhea if this condition is present. These effective steroidal compounds suppress the release of gonadotropins and stop the estrous cycle by preventing follicle formation, ovulation and the formation of corpora lutea.

Less research has been done with the use of steroids as contraceptive agents in queens. The administration of progestational compounds in cats causes less uterine disease than in dogs. Mibolerone (19-norandrogen) is not approved for use in the queen, although daily oral doses of 50 ug prevent estrus.^{3,4} These and even smaller doses cause thyroid dysfunction, clitoral hypertrophy and hepatic dysfunction. Megestrol acetate (**Ovaban**) at a dose of 5 mg/day for 3 days and then 2.5 to 5 mg/week has suppressed estrus in young queens for over a year. Even queens in estrus will go out of estrus after 3 days on megestrol acetate. This product should not be used in cats with infections of the genital tract.⁹ Since the queen is an induced ovulator, one can apply coital stimulus with a vasectomized tom cat or a pseudocoital stimulus with a sterile rod or swab inserted into the vagina during estrus. Also 25 units of HCG (human chorionic gonadotropin) per lb. of body weight can be administered to induce ovulation which is followed by a diestrus or pseudopregnancy that lasts for 35 to 45 days.^{3,5} Progesterone-like agents used for prolonged periods in dogs have produced cystic degeneration of the endometrium and secondary endometritis and pyometra. They are of no value

in preventing conception after coitus, in fact some of these agents actually promote conception and maintenance of pregnancy if given at this time.

Experimentally in cattle the injection of oxytocin, 100 to 200 I.U. daily from day 2 to day 7 after estrus causes an inhibition of the growth and development of the corpus luteum and its secretion of progesterone necessary to maintain pregnancy. Usually cattle treated in such a manner return to estrus in 8 to 10 days. Thus this treatment should also prevent conception in bovine animals bred accidentally.

In areas such as India where bulls and cows are not confined and the amount of feed available is limited, the value of a small stainless steel spring similar to a "bobby pin" inserted into the cervix of a heifer or cow and remaining indefinitely has been demonstrated.¹¹ Although under these conditions estrous cycles, coitus and conception may occur, abortion results due to the failure of the cervix to be able to seal itself properly. This technique was an early application of the presently widely accepted intrauterine devices (I.U.D.) used in women to prevent conception. Depending upon the species of animals the I.U.D.'s prevent fertilization, prevent implantation or interfere with normal corpus luteum development.

Intravaginal or preputial devices to prevent conception have not proven satisfactory for general use.³ Ovariectomy effectively suppresses the estrous cycle and together with castration or vasectomy prevents conception in all domestic animals.

The induction of abortion in domestic animals following conception can be accomplished in a variety of ways depending on the species of animal, the duration of pregnancy, the desires of the owner and the ease of inducing abortions by physical, hormonal or surgical procedures. Generally the earlier in gestation an abortion is induced, the simpler and easier it is for the dam and the veterinarian and fewer complications will arise. Inducing abortion after midgestation or early in the third trimester should generally be discouraged because of the difficulties in the induction and the problems of delivery and aftercare of the dam. (See Induction of Parturition.)

Douching the uterus by means of a catheter or pipette with antiseptics such as 1 to 2 percent Lugol's solution, 200 ppm. chlorine solution, dilute acetic acid or 2 to 3 percent potassium permanganate solution or even saline 7 to 20 days or longer after service in the cow or mare, is often successful, possibly by also introducing bacteria to cause an endometritis, and destroying or expelling the developing ovum or embryo. Injecting of irritating solutions such as dilute Lugol's solution around the third to sixth day after service in the cow may result in similar changes as produced by the injection of oxytocin with a

shortened time between estrous periods due to the release of prostaglandins from the endometrium resulting in luteolysis. In mares abortion may be produced readily up to 8 months of gestation by manual dilation of the cervix in a sterile manner and injecting several hundred ml. of dilute Lugol's solution or other suitable mild antiseptic. One author¹⁴ aborted over 100 army remount mares by injecting 500 ml of sterile iodized oil or physiological saline into the gravid uterus. Possibly manual dilation alone would be sufficient in the mare. Aborting mares with fetuses over 8 months of age may cause injury or result in infection or dystocia in the mare. Douching the uterus and dilating the cervix is not practical or possible in the ewe, bitch, sow or cat.

Injection of hormones to induce abortion has been reported in all species of domestic animals. The usual hormones used in early to midgestation are estrogens, prostaglandins and possibly cortisone (dexamethasone). The use of these hormones for inducing abortion has been described previously in this Chapter under abortion in the various species. Often a combination of several hormones is superior to a single product. Following these treatments the veterinarian should follow each case to be certain abortion occurred and no complications such as dystocia, fetal maceration or uterine infection developed.

Although seldom used at this time manual **removal of the corpus luteum of pregnancy** in the cow per rectum invariably results in abortion in about 3 to 5 days. Since there is some danger of hemorrhage and ovarian and uterine adhesions following manual removal or enucleation of the corpus luteum in the cow, and early involution and luteolysis is readily produced by estrogens and prostaglandins, the latter products have replaced the former hazardous procedure. Removal of the corpus luteum during early pregnancy in the mare or other domestic animals is not possible except by laparotomy and ovariectomy.

Manual rupture of the amnionic vesicle in the cow and the chorionic vesicle in the mare with destruction of the embryo or fetus is possibly by digital manipulation through the rectal wall from 30 to 100 days of pregnancy in the cow and 17 to 40 days in the mare as described previously under physical causes of abortion in the cow and mare. It was interesting to note that in single bovine pregnancies when the embryo was destroyed that "pregnancy" continued and the membranes grew for 2 to 3 weeks following the rupture of the amnionic vesicle.^{1,2} Estrus seldom occurred until 30 or more days after inducing embryonic death.^{1,2,13} Manual destruction of one of twin embryos was reported to be successful in the mare⁶ but in the cow when one embryo was manually

destroyed, the other also succumbed.¹³

The re-establishment of a normal estrous cycle within 2 or 3 months in the mare after terminating pregnancy after 40 or more days of gestation is very unlikely. The endometrial cups and their secretion of PMSG have an adverse effect on the initiation of normal follicle development, ovulation and the normal expression of regular periodic estrous signs in the mare.

The timed induction of parturition in the later stages of pregnancy by the use of glucocorticoids and prostaglandins in cows, sows, ewes and does, and oxytocin in mares have been described briefly under abortion in the various species and will be discussed in greater detail under parturition.

Prevention of Conception and Induced Abortion

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Extrauterine Pregnancies and Fetuses

True Extrauterine Pregnancy is characterized by a fertilized ovum, embryo, or fetus that has established nutritive relations with organs or tissues other than the endometrium and has undergone in this location a degree

of embryological development. In humans ovarian and tubal pregnancies may occur, the latter being fairly common. True abdominal pregnancies, with the fetal placenta attaching to the mesentery and omentum, have been described as rarely occurring in humans. In ovarian, tubal, and abdominal pregnancies the embryonic development proceeds only a short time and then the fetus succumbs. In human tubal pregnancy the oviduct ruptures, usually accompanied by severe hemorrhage. No authentic cases of true extrauterine pregnancies have been described in domestic animals. This difference is apparently related to the manner in which the developing zygote establishes nutritive relationships with the dam. In humans and rodents the developing zygote erodes the mucosa and buries itself in the maternal tissues while in domestic animals the villi of the trophoblast attach themselves in the maternal crypts formed in the endometrium.

False or Secondary Extrauterine Pregnancy is seen occasionally in all domestic animals and very rarely in the mare.² In this condition the fertilized ovum, embryo, or fetus develops normal placental relationships with the endometrium and the fetus reaches recognizable size. It then escapes from the uterine cavity into the abdominal cavity. This condition usually occurs the last two-thirds of the gestation period. Almost all secondary extrauterine fetuses are dead by the time the condition is diagnosed. The cause for uterine rupture, allowing the escape of the fetus into the abdominal cavity, is frequently unknown. The condition is seen in uterine torsion, fetal emphysema, chronic perimetritis with adhesions and following dystocia and oxytocin administration especially in the bitch.^{3,4} It may occur spontaneously or possibly associated with violence or trauma in advanced pregnancy. In multipara, uterine torsion may involve a part of one horn or the entire horn with the enclosed fetuses being separated from the rest of the uterus. The adhesions that take place may cause the condition to be diagnosed as an extrauterine pregnancy or fetus. In many cases in domestic animals in which a sterile fetus is released into the abdominal cavity little or no external symptoms may be evident. The fetus dies and with its membranes becomes walled off as a sterile foreign body in the ventral portion of the abdominal cavity and remains there as an inert mass for months.^{1,6,7} Often extensive adhesions between it and other abdominal viscera develop. The site of the rupture may only be a small or invisible scar after the uterus involutes. Since most of these fetuses are well-walled off, no external symptoms are usually seen. Occasionally mild digestive disturbances may be evident. In rare cases a large extrauterine fetus may be diagnosed on rectal examination in the cow if the fetus was near term when it escaped from the uterus.

A differential diagnosis must be made, considering mummification of the fetus, tumors, and fat necrosis. Diagnosis of most cases in the larger domestic animals is made at the time of slaughter. In the dog and cat abdominal palpation, radiographs and exploratory laparotomy may aid in revealing the extrauterine fetus(es) especially in an ailing animal soon after parturition. Reports would indicate that secondary extrauterine pregnancy and extrauterine fetuses occur more commonly in queens than in bitches.^{1,6} These fetuses may be or become infected, macerate, cause peritonitis and the death of the dam or rarely be walled-off and be expelled into the alimentary tract or through the abdominal wall.^{3,8}

If extrauterine fetuses are diagnosed in large animals the prognosis is guarded and the animal is usually slaughtered. A laparotomy operation to remove the extrauterine fetus would be difficult and many adhesions would remain. In the dog and cat an operation might be considered in cases of chronic, walled-off extrauterine fetuses.

In animals with uterine rupture late in pregnancy or at the time of parturition, secondary to trauma, torsion, fetal emphysema or possibly spontaneous rupture, the fetus and uterine contents escape into the abdominal cavity. If the fetus is emphysematous or grossly infected, fatal peritonitis and shock frequently follow. In rare cases the fetus may still be found alive and the dam and possibly the young can be saved by an immediate laparotomy to remove the dead or live fetuses and repair the ruptured uterus.

In the mare a rotated or compound bicornual pregnancy may be confused with an extrauterine fetus. In this condition the birth passageway is very long and the fetus may be palpated beneath the stretched vagina and uterine body and simulate an extrauterine fetus. In humans some long-existing extrauterine fetuses become quite firm and encapsulated with calcium laid down in the capsule, causing them to be spoken of as lithopedions. These well-encapsulated extrauterine fetuses in animals may occasionally be referred to as extrauterine fetal mummies.

Dropsy of the Fetal Membranes and Fetus

These pathologic conditions in pregnant domestic animals may include hydramnios, hydrallantois, edema of the allantois chorion, fetal anasarca, or fetal edema with ascites and hydrothorax. These conditions are usually found singly but on rare occasions may be associated. In hydramnios and hydrallantois in uniparous animals the abdomen is usually distended as if twins or triplets are present. All cows in which twins are suspected should

be examined promptly for these possible dropsical conditions. Of these conditions hydramnios and hydrallantois are most common with the latter occurring 10 to 15 times more frequently than the former. In 7 percent of cases both hydramnios and hydrallantois were present together.²³

Hydramnios or hydrops of the amnion is characterized by a gradual enlargement or filling of the amniotic cavity that is associated with a genetic or congenitally defective fetus. The condition is seen most commonly in cattle, occasionally in sheep, rarely in pigs and carnivores, and it has not been reported in horses.³ It may affect one of twin fetuses. At midgestation the amniotic fluid is watery and slightly yellow and in normal bovine conceptuses only increases in amount very slowly until the last month of pregnancy when it nearly doubles in amount.^{1,3,4} In normal sheep there is a sudden increase around the 100th day of pregnancy. From mid-gestation onward the amniotic fluid becomes more viscid and glairy because the early watery fluid is swallowed or possibly inhaled into the large bronchi and absorbed and a large volume of saliva is continually produced. In defective fetuses swallowing is impaired and the amounts of amniotic fluid increase gradually to 5 to 30 gallons. Hydramnios is not solely due to a failure of deglutition in the fetus as other mechanisms besides swallowing regulate the volume and composition of amniotic fluid.²⁵ During the last few months of gestation, when hydramnios becomes apparent, the amount of amniotic fluid in normal cows is only 1 to 2 gallons.

Genetic or hereditary conditions resulting in defective fetuses often associated with hydramnios are: 1) Dexter cattle pregnant with "bull dog" calves. In these animals the disease is apparent at 3 to 4 months of pregnancy.⁷



Figure 77. Jersey cow about 7 to 8 months pregnant affected with hydrops and a transverse rupture of the abdominal muscles 8 inches cranial to the pubis. The cow was unable to stand.

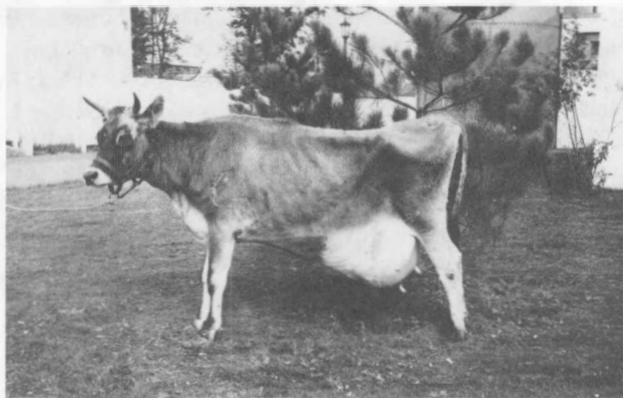


Figure 78. Same Jersey cow with marked ventral hernia with signs of rupture of the prepubic tendon two weeks after a cesarean section.

2) Angus cattle pregnant with small brachygnathic, defective calves with osteopetrosis. These exhibit increased abdominal enlargement the last month of gestation. 3) A muscle contracture monster associated with hydrops of the amnion has been described in Red-Danish cattle.¹² 4) Prolonged gestation in Guernsey cattle characterized by an immature defective small fetus with pituitary hypoplasia or aplasia may be associated with hydramnios. 5) A lethal muscle contracture monster in sheep accompanied by dropsy of the amnion has been described.¹⁸ Hydramnios was commonly observed with hydrocephalic fetuses in Hereford cattle.^{5a} All of the above defective fetuses have been caused by recessive autosomal genes (See chapter on Anomalies of the Fetus). Hydramnios is also seen in cattle with congenitally anomalous fetuses such as conjoined twin monsters, **Schistosomus reflexus**, and fetuses with anomalies of the cranial portions of the body. Hybrids produced by mating of an American bison bull with a domestic cow resulted in hydrops of the amnion.²⁴ Anencephaly is frequently the cause of hydramnios in women.⁶

Hydramnios develops slowly over several months during the latter half of pregnancy. If the condition causes obvious abdominal enlargement it is usually the last month or six weeks of the gestation period. Often the condition is not recognized until parturition when large quantities of syrupy, viscid amniotic fluid, occasionally containing meconium, is released. The differential diagnosis between hydramnios and hydrallantois has been described. (See Table 14.) The prognosis for the future breeding life of the dam is fair to good in hydramnios but the fetus is invariably defective and dies. Retention of the placenta and metritis are not serious problems as with hydrallantois. Abortions and premature parturitions are frequent in cases of hydramnios. Because of the enlarged

Table 14. The Differential Diagnosis Between Hydrallantois and Hydramnios in Cattle

Hydrallantois	Hydramnios
Occurs in 85 to 90% of cases of uterine dropsy.	Occurs in 5 to 10% of cases of uterine dropsy.
Abdominal enlargement develops rapidly within 5 to 20 days.	Abdominal enlargement develops slowly over weeks and months.
Abdominal wall is round, distended and tense.	Abdominal wall is pear-shaped and less tense.
Distended horns of uterus easily palpated per rectum and fill the abdominal cavity.	Uterine horns hard to palpate, not very tense and don't fill the upper and caudal abdominal cavity area.
Fetus and placentomes are not able to be palpated or ballotted per rectum or through the abdominal wall.	Placentomes and often the fetus may be palpated per rectum and the latter may occasionally be ballotted through the abdominal wall.
Sporadic in incidence.	Usually sporadic but in an inbred herd may have a number of cases.
Allantoic fluid is watery, clear and amber, with characteristics of a transudate.	Amniotic fluid usually syrupy and viscid, and often contains meconium.
Fetuses are normal but small twins are occasionally present.	Associated with a defective, small, anomalous fetus.
Placenta, especially the allantois chorion, is usually diseased and abnormal with a reduced number of greatly hypertrophied placentomes.	Placenta, allantois chorion and placentomes normal.
After removing much fluid by caesarean section or by allantocentesis, the allantoic cavity rapidly fills again.	After removing much fluid by caesarean section or by amniocentesis, the amnion does not refill in the former and only slowly in the latter.
Retained placenta and severe metritis usually occurs.	Retained placenta may occasionally occur and metritis is much less common or severe.
Sequelae such as uterine rupture, abdominal hernias and dislocation of the hips are common in severe cases.	Adverse sequelae are rare due to gradual onset and the nature of the disease.
Prognosis—guarded to poor for life and fertility.	Prognosis—fair to good for life and fertility.

uterus, uterine inertia, and defective fetuses, dystocia at parturition is not uncommon. It is usually easily handled because of the small size of the fetus. In hydramnios associated with prolonged gestation and fetuses with defective or missing pituitary glands injections of large repeated doses of glucocorticoids, prostaglandins, and estrogens might be indicated to produce abortion or parturition. If the fetus is dead, glucocorticoids are of questionable value.^{4,19,21} Combinations of these hormones may avoid repeated large doses of a single hormone. Further trials are indicated. Cesarean section, as described under hydrallantois, can also be used to terminate a pregnancy with hydramnios. The genetic implication in salvaging an affected dam should be considered. If the defective fetus and hydramnios is due to a recessive gene then the dam and sire are carriers. Such animals should be eliminated from the herd and any inbreeding in the herd should be discouraged.

Hydrallantois, dropsy or hydrops of the allantois, is the single factor present in 85 to 90 percent of the dropsical conditions affecting the bovine fetus and its membranes. This condition is seen sporadically in dairy and beef cattle. It is often associated with a diseased uterus in which most of the caruncles in one horn are

not functional and the rest of the placentomes are greatly enlarged and possibly diseased. Adventitious placenta are commonly observed. Portions of the placenta may be necrotic and edematous. Hydrallantois is seen quite commonly in cattle carrying twin fetuses or greater multiples. Hydrallantois apparently is caused by structural or functional changes in the allantois chorion including its vessels with transudation and collection of fluid, differing from normal allantoic fluid but resembling plasma.²⁰ One may remove many gallons of this transudate from the allantoic cavity with a trocar but within 2 to 4 days it has been restored. This would tend to indicate that the fetal kidneys probably seldom play a role in causing this disease. The presence of cystic kidneys, hydronephrosis, or dysfunction of the fetal renal tubules resulting in polyuria might be concerned in the pathogenesis of hydrallantois.¹⁶ The author has seldom observed such abnormalities in the fetal kidneys of fetuses from affected cows and further suggests these changes are probably secondary to the hydrallantois. Torsion of the uterus and torsion of the umbilical cord are not associated with this condition. The navel cord in the cow is short and seldom twisted. In the mare torsion of the umbilical cord may occur and be severe enough to cause the death of the

fetus but dropsy of the fetal membranes and fetus rarely occur. The author and others have observed mares with hydrops allantois that spontaneously aborted a small defective fetus. In one case there was evidence of moderate umbilical torsion with an area of adhesion between the amnion and chorioallantois. This condition appeared to be more prevalent in cattle in seasons when forage has been damaged, with a possible loss of vitamin A resulting in a lowered resistance of the endometrium to disease.^{13,24} In cases of hydrallantois associated with a reduced number of placentomes and uterine disease the fetuses are usually growth-retarded and show some edema and ascites. Hydrallantois usually affects cows 3 or more years of age although rarely the condition may be seen in heifers in which possibly a congenital lack of uterine caruncles was present. In older cows this lack of caruncles characteristic of hydrallantois may be due to prior uterine infection or even tuberculous metritis.³

The signs of dropsy of the allantois vary depending on the degree of the involvement and the stage of pregnancy. In mild cases, where the amount of fluids is moderate, 10 to 20 gallons, the condition may not be diagnosed until parturition. At this time an excessive amount of clear, watery, amber fluid with the characteristics of a transudate is expelled. The fetal membranes may be tough and rupture with difficulty. The uterus is greatly enlarged and atonic and the small, growth-retarded fetus may exhibit some edema and ascites. Dystocia may result at the time of abortion or parturition due to uterine inertia. The fetus is usually dead at birth or dies shortly thereafter. Retention of the fetal membranes and septic metritis are common sequelae to this dropsical condition. In severe cases, symptoms of hydrops of allantois may occur as early as the fifth month of pregnancy but nearly all cases develop the last 3 months of gestation.⁴ Hydrallantois usually develops rapidly within 5 to 20 days and is characterized by a distended uterus and enlarged abdomen (See Figure 77). Spontaneous abortion at 6 to 9 months may frequently be observed.^{21,23} In the more severe cases the amounts of fluid may reach 30 to 60 gallons. The fetal membranes may be heavy and edematous and the cow frequently has ascitic fluid in her abdominal cavity. Thus the weights of the dropsical fluids, membranes, and uterus frequently total 350 to 550 lbs. This excessive volume of fluid distending the abdomen causes the owner to believe his records of breeding dates are wrong or else the cow is going to have triplets. Later, digestive symptoms with anorexia, lack of ruminations, and constipation are noted. The condition is frequently misdiagnosed as indigestion, bloat, or traumatic gastritis. The cow may drink excessive amounts of water. The temperature is normal. The pulse is elevated to 90 to 140

per minute and is weak and wiry. The cow may exhibit anxiety, restlessness, and an expiratory grunt. Because of the excessive volume of fluid, the fetus can seldom be ballotted or felt per rectum. On rectal examination the uterus is greatly distended and tense. Placentomes can seldom be felt, due to the tense uterine wall, but the uterine arteries are "whirring" indicative of a live fetus. The uterus appears to fill the abdominal cavity. As the condition progresses—and it may progress quite rapidly at any time during the last trimester of pregnancy—the abdomen becomes more distended. The gait is stiff, slow, and cautious. The cow loses body condition, and eventually is unable to rise. Dislocation of the hips or backward extension of the rear limbs may occur and the cow lies on her sternum looking like a "bloated bull frog" (See Figure 77). Rarely in the cow and mare rupture of the prepubic tendon or ventral hernia may occur due to the excessive weight of the uterus. Rupture of the uterine wall has also been described.^{9,17,23} For a differential diagnosis between bovine hydrallantois and hydramnios see Table 14.

In mares hydrops allantois is rare.²² It may occur in mares of any age. The condition becomes evident the last trimester of gestation with signs similar to those observed in cows. Dystocia and retained placenta secondary to the uterine inertia caused by the greatly distended uterus is common. The fetus in affected mares is often defective, growth retarded and some may exhibit hydrocephalus but while most all are alive at delivery, they invariably die within a short time. Other dropsical conditions affecting the fetus are much less common.

Edema of the allantois chorion characterized by extensive and severe edema distending these tissues to a thickness of 4 to 6 inches has been associated with **Brucella abortus** infection causing placental disease in cattle and therefore is rarely seen at present in the United States. Hydrallantois is rarely associated with **Brucella abortus** infection.

Fetal ascites severe enough to cause dystocia may also rarely be due to **Br. abortus** infection. Slight fetal ascites and edema as well as mild placental edema is frequently associated with intrauterine fetal death and sterile autolytic changes.

Fetal anasarca or excessive edema of fetus is seen most commonly in cattle but may affect sheep. It may develop in a single fetus or one of twins. It is also rarely observed in one or two of a litter in swine or carnivores. Rarely mild hydrops of the amnion and/or allantois and edema of the placenta may accompany fetal anasarca. Abortions of affected fetuses are fairly common from 4 to 8 months of gestation in uniparous animals. The condition has been described affecting Ayrshire cattle.⁸ This

is caused by a recessive autosomal character. Most anasarctic fetuses were expelled dead. In all of these latter conditions with the possible exception of edema of the allantois chorion, enlargement of the abdomen is not noted.

The prognosis for hydramnios is fair to good for the dam unless she is a carrier of a recessive gene responsible for the defective fetus producing the condition. Salvage of the defective fetus is usually impossible. In many of these cases following induced abortions or caesarean section the placenta is often expelled or if it is retained, metritis associated with uterine inertia is not as severe as that following hydrallantois. The prognosis in cases of hydrallantois is poor. In advanced cases in which the cow is unable to rise, the prognosis is often hopeless. Even if the fetus can be removed, the mortality in cows is high, because the uterus is very atonic, the membranes diseased, and shock or severe septic metritis usually follows the expulsion or removal of the fetus. If the cow should survive, its future reproductive life is questionable. In almost all cows with hydrops except the occasional slight or moderate one that goes to term and spontaneously delivers, the fetus dies *in utero* or soon after birth. Milk production in dairy cows for the next lactation after either hydramnios or hydrallantois is usually poor. Dropsy of the allantois at term is often associated with dystocia due to a dead edematous fetus in an abnormal position or posture, uterine inertia, and a cervix that may fail to dilate completely. If the dystocia is not handled promptly emphysema of the fetus soon develops. In the rare cases of hydrops allantois seen in mares the prognosis is guarded but better than in cattle unless rupture of the prepubic tendon occurs. The prognosis in rare cases of edema of the allantois chorion is similar to hydrops allantois. In both severe fetal ascites and fetal anasarca, dystocia usually results at the time the overly large fetus enters the birth canal, whether the fetus is aborted or expelled at term.

The treatment or handling of cases of hydramnios and hydrallantois varies with the duration and severity of the condition. In mild cases undiagnosed until the time of abortion, premature birth or at normal parturition, excessive volumes of fluids are observed accompanied by the presence of a poorly viable, small, growth-retarded or defective fetus, dystocia related to the diseased or dead fetus, and uterine inertia secondary to the uterine distention. Mutation and forced extraction of these fetuses is usually easily effected. In mares about one-half of the cases terminate by spontaneous abortion or birth at or near term.²² In cases of fetal anasarca or ascites greater amounts of traction and lubrication may be needed. In a few cases fetotomy might have to be resorted to in

order to mutilate the fetus to allow the excess fluid to escape. Retained placenta and a secondary severe metritis frequently follows hydrallantois and edema of the allantois chorion but is less frequently observed and is less severe in hydramnios. Early treatment for these conditions with parenteral and local antibiotics and ecbolics such as oxytocin, stilbestrol and ergonovine are indicated.

In severe cases of hydramnios and hydrallantois occurring during the gestation period with a closed cervix, the prompt termination of the abnormal pregnancy is usually desired. In some slowly developing cases late in gestation it may be expedient to observe the cow or mare and wait for or induce parturition. In other severe cases an early decision to slaughter the cow while she is still in good physical condition is often the best method of handling these cases when all factors are considered. Daily administration of large doses of stilbestrol, 50 to 120 mg., or estradiol, 8 to 10 mg. for 4 to 7 days alone or together with large doses of prostaglandins, and glucocorticoids and antibiotics may frequently result in cervical dilation and abortion.^{4,14,15,19,21,23} Precipitating abortion is more successful with hydramnios than hydrallantois. Because the uterus is atonic and distended and the cervix usually dilates poorly, the cow should be watched carefully. The abortion should be aided when necessary. Pituitrin or oxytocin may be given but its effect may be negligible because of the atonic, stretched, and diseased uterine wall.

In the mare abortion or premature birth may be induced by manual dilation of the cervix, rupture of the usually thick, tough allantois-chorion and very slow drainage of the allantoic fluid to prevent shock. Oxytocin, 50 units, in a liter of saline given slowly intravenously, and repeated if necessary, to aid uterine contraction and delivery as well as promote expulsion of the placenta has been recommended.²² Injection of estradiol, 20 mg., 24 hours before induction of abortion might be indicated to promote relaxation of the cervix and genital tract. Manual removal of the fetus is usually necessary. Cesarean section has been attempted in many cases with success but in some the cow succumbs. Various authors^{5b,10,16} have recommended the use of a sterile trocar or plastic tube inserted by a surgical procedure through the abdominal and uterine walls to draw the fluid off gradually at a rate of one liter per minute before the Cesarean is performed. This helped to avoid possible shock from removing too much fluid too rapidly. The draining of 25 to 50 liters of allantoic fluid often induces abortion within one to three days. In a few cases it may be indicated to repeat this treatment.^{5b} Since most severely affected cows are very dehydrated with marked electro-

lyte imbalances, appropriate fluid therapy in large volumes is indicated before, during and after the operation. Once the cow is down and unable to rise due to the weight of the fluid, any treatment is usually unsuccessful because of complications such as abdominal hernia, severe myositis and nerve damage or dislocated hips. Following the relief of these severe dropsical conditions metritis usually associated with retained placenta almost invariably follows. The severity of this metritis varies with the severity of the condition and is a common cause for the high mortality. In all hydrops cases the treatment for septic metritis should begin before or at the time the condition is relieved with supportive fluid therapy, antibiotics, both parenteral and locally in the uterus and frequent injections of ecbolics. Since treatment of this condition is not very successful, most of the more severe cases are sent to slaughter as soon as they are diagnosed. This is especially true if the cow is of only moderate value. Three cases of hydrops allantois were successfully corrected by Cesarean section after slowly draining off 20 to 30 gallons of allantoic fluid in the one-half hour before the Cesarean operation.^{4b} The pulse and respirations were monitored and Ringer's solution with dextrose was administered intravenously during the operation. Subsequent treatment with estrogens, antibiotics and further supportive therapy was necessary to control metritis as the placenta was retained for up to three weeks. It was recommended that the cows not be rebred. If more than 1 or 2 cases of hydramnios occur in a herd the hereditary nature of this disease should be suspected and investigated, and further inbreeding prevented.

An interesting observation is that after terminating hydrops of the allantois by cesarean section the uterus may continue to fill with transudative fluid for about 48 hours and require further draining.¹⁵

Abdominal Hernias Resulting in Hysterocele

The pregnant uterus may drop into, or be present in, umbilical, inguinal, perineal, diaphragmatic, or ventral hernias. In cases of rupture of the prepubic tendon, the pregnant uterus will drop into the sac formed by the skin and cutaneous muscles. This may cause dystocia or death of the fetuses or dam or both.

Umbilical and inguinal hernias may, if large enough, contain a portion of the uterine horn and developing fetus. **Umbilical hernias** have been described as hereditary in all species of animals. In cows most of them are small. Such animals should not be used as breeding animals. Umbilical hernia in cattle, especially Holsteins, is probably an autosomal dominant with low pene-

trance.^{4b} Most female animals with large umbilical hernias are not bred. In males an umbilical hernia may prevent copulation. **Inguinal hernias** are hereditary or acquired and are described as common in the bitch, and rare in the queen, sow and mare. They have not been described in the cow or ewe. Bitches over 5 years of age are most commonly affected.¹⁰ Spayed bitches given large amounts of estrogen developed inguinal hernias within 90 days.⁸ One bitch with an inguinal hernia was spayed through a midline incision and the hernia was left intact. One year later the hernia had spontaneously disappeared. These observations indicate a close relationship between estrogen production by the ovary and the development of inguinal hernia in bitches. Inguinal hernias may be bilateral or unilateral, usually the latter, and are characterized by a swelling in the inguinal region. This becomes larger as pregnancy progresses if a portion of the pregnant uterine horn is present in the hernial sac. In the bitch one to three fetuses may develop in the hernial sac. If pregnancy is allowed to progress it results in the death of the fetuses or in dystocia at the time of parturition. In the bitch this condition should be differentiated from a mammary neoplasm and a local abscess. **Diaphragmatic hernia** is usually secondary to trauma in the bitch and other multiparous female animals and in rare cases a pregnant uterine horn may be present in the thoracic cavity.^{6,9} A **perineal hernia** containing a portion of the fetus has been described in the goat.¹ **Ventral hernias** are usually traumatic in origin and may occur in all species. In the mare they may occur at the time of parturition in the caudal, ventral abdominal area just lateral to the midline. If possible, surgical repair should be delayed several months or more until the edges of the hernial rupture have healed and organized.⁷ If they are large a portion of the uterine horn and fetus may develop therein. If ventral hernias in large animals are extensive they are difficult if not impossible to repair. Fortunately, in large animals the uterus in early pregnancy does not drop far enough downward or forward to drop into most hernial sacs and in later pregnancy the uterus is too large to enter them.

In the bitch, an inguinal hernia containing a portion of a pregnant horn can be handled surgically early in pregnancy by reducing and repairing the hernia, if necessary by enlarging the ring and/or using a synthetic mesh for a lasting support. From midpregnancy to near term, hysterotomy can be performed and the fetus or fetuses removed, the uterus replaced in the abdominal cavity, and the hernial ring sutured. Occasionally the portion of the herniated uterine horn containing fetuses may be removed by a partial hysterectomy. In other cases ovari-hysterectomy may be indicated. The rare cases of um-

bilical or ventral, diaphragmatic or perineal hernias encountered containing a portion of the pregnant uterus could be handled in a manner similar to the repair of inguinal hernias.

Extensive unilateral ventral hernias in large animals occur occasionally in advanced pregnancy in cows, ewes, and does, but rarely in mares. These hernias are usually due to trauma. The greatly increased weight of the gravid uterus and fetus, and possibly other changes, weaken the abdominal floor. These extensive hernias are seen most commonly in ruminants on the right side of the abdominal floor. They are observed most often on the left side in the mare.² In rare instances they may be associated with twins or greater multiples or with hydrops of the amnion and allantois. Large unilateral ventral hernias are characterized by a unilateral ventral sagging of the abdominal floor, 6 to 8 inches or more below that of the normal side. Calving or foaling may be difficult because of the inability of the abdominal muscles to contract equally and strongly and force the fetus toward and through the birth canal. Following calving, the abdominal floor of the affected side may retract in some cattle and the abdominal contour become nearly normal. This may occasionally remain normal during subsequent pregnancies. However, it usually recurs during the latter stage of each gestation period. The involvement is so great that treatment or operations other than those outlined under rupture of the prepubic tendon are not indicated.

Rupture of the prepubic tendon or prepubic desmorrhaxis of pregnancy is seen most commonly in the mare, and rarely in the cow and ewe. This condition is seen most frequently in the draft mare that is idle and well-fed, and infrequently in light mares. It is rare in

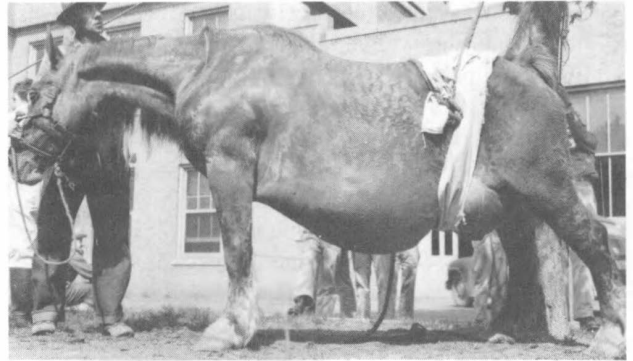


Figure 80. Acute rupture of the prepubic tendon in a mare.

cattle because the subpubic tendon, a structure that does not exist in horses, gives added support to the prepubic tendon.⁴ (See Figures 78, 79, 80.) Rupture of the prepubic tendon occurs during the last 2 months of gestation. In the mare and occasionally the cow it is often preceded by a marked tense, painful edema, 6 to 14 cm. thick, on the abdominal floor, starting at the udder and extending to the xiphoid region. Severe edema of the abdominal floor in the mare in advanced pregnancy should always be viewed seriously. Physiological edema of the abdominal floor in the cow is common and does not indicate a possible weakness or rupture of the abdominal floor as in the mare. Rarely massive hematomas in the region of the bovine udder may be mistaken for rupture of the prepubic tendon.⁵ (See Figure 81.)

The rupture is predisposed by the increased weight of the gravid uterus on the abdominal floor and possible degenerative changes due to the edema and the weight. Occasionally, due to violence or trauma, the condition

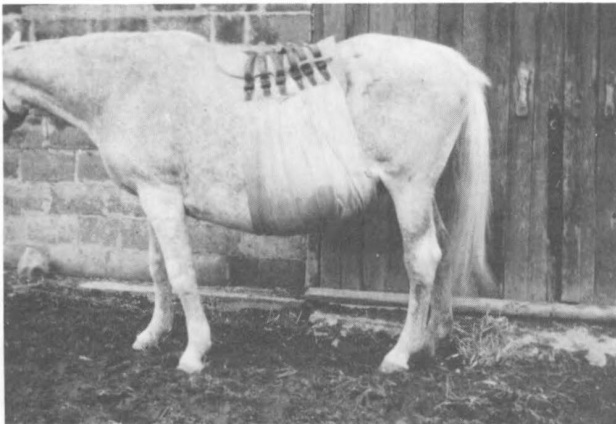


Figure 79. Impending rupture of the prepubic tendon in an old mare. A proper support has been applied.



Figure 81. A massive hematoma cranial and dorsal to the mammary gland of a pregnant cow resembling a rupture of the prepubic tendon.

occurs suddenly without the development of edema. Twins or greater multiples,³ hydrops of the fetal membranes, fetal giants in prolonged gestation, as in *Veratrum* poisoning in ewes, favor rupture. In this condition there is a transverse rupture of the prepubic tendon, the ventral abdominal muscles, abdominal tunic, and peritoneum letting the viscera and gravid uterus drop downward into a sac formed by the skin and cutaneous muscles. Only very rarely does complete eventration occur. In rupture that occurs suddenly due to violence, besides the sudden enlargement in the ventral abdominal region and the sinking of the flanks, there usually occurs intense pain and colic together with a cold sweat, fast respirations, rapid weak pulse, and a tendency toward collapse due to shock, and possible hemorrhage (see Figure 80). Occasionally a mare and her intrauterine fetus will perish at this time despite supportive treatment of blood, saline, stimulants, and support for the abdominal wall. In most cases the onset is more gradual, with a preceding painful edema of the abdominal floor, a stiff, careful, cautious gait, and refusal to lie down. After rupture has occurred the udder and teats are stretched forward and downward on the abdominal floor. The attitude is a typical "saw-horse" one, with an elevation of the tail head and the ischial tuberosities and a lordosis. The pelvis is tilted backward because the prepubic tendon is not intact to maintain the pelvis in its proper relationship to the spinal column.

The prognosis in rupture of the prepubic tendon is always poor, as most mares and foals succumb before foaling occurs. If foaling should terminate successfully the mare's condition will improve, and she might do light work; but usually the mare is so unsightly that she is destroyed. Rebreeding these mares is definitely not indicated. Affected cows are usually sold after calving and lactation because of difficulty in milking and because rebreeding is contraindicated.

Treatment is usually unsatisfactory, once rupture of the tendon has occurred. Preventive treatment of mares showing marked edema of the ventral abdominal floor and a stiff cautious gait should consist of confining the mare in a large comfortable box stall and restricting exercise. Large bulky feeds should be withheld and a light concentrate ration should be fed. In some mares mild laxatives might be indicated. A suitable heavy, wide canvas webbing should be tightened securely with straps around the abdomen, to transfer the weight of the abdominal viscera to the spine. Padding over the back usually is necessary to prevent pressure necrosis. (See Figure 79.) The mare should be watched closely for the beginning of parturition so that aid may be given at once and the fetus withdrawn by traction. This aid is neces-

sary since abdominal contractions are very weak and parturition cannot take place without aid and direction. In most cases uterine contractions and cervical dilation may take place but since the fetus does not engage or enter into the pelvic cavity, abdominal contractions, or labor do not begin. Periodic vaginal examinations may be necessary. In some cases the wide band in a horse sling to support the abdominal viscera may be useful and the mare can be kept standing. Possibly parturition should be induced in the mare in late pregnancy by the injection of estradiol and 30 to 40 units of oxytocin. Another possibility in these mares is cesarean section which, though often successful permits the fetus to be saved, while the affected mare is usually destroyed. This latter procedure is indicated in sudden rupture, with impending collapse and death of the mare. In the cow abdominal support or slings are not tolerated. Induction of premature birth by the administration of large, repeated doses of glucocorticoids, prostaglandins and estrogens in the cow is usually successfully accomplished with fewer complications than a cesarean operation. By confinement and careful observation, the fetus may be promptly withdrawn by traction. In the cow cesarean section is more successful than in the mare and may occasionally be indicated in this condition. In relieving dystocia due to rupture of the prepubic tendon, rolling the cow or mare on its side or back will aid in bringing the fetus to the pelvic inlet for removal. If the mare is in a standing position, horse slings may be applied and tightened to bring the fetus near the pelvic inlet.

Torsion of the Uterus

Torsion of the uterus may occur in all species of animals. Uterine torsion is usually defined as the revolution or twisting of the uterus on its long axis. This might be true in the mare, where torsion of the uterus is uncommon due to the dorsally attached broad ligaments that tend to prevent torsion. In other species of animals such as the cow, ewe, and doe, the gravid horn is in the shape of an arc or a U-shaped loop with the vagina and ovary at the respective ends of the arc. Torsion involves the rotation of this arc on its transverse axis, similar to an intestinal volvulus. This same type of torsion occurs in multipara when one horn rotates at its base. A modification of this same volvulus type of torsion occurs in multipara when only a portion of one horn, containing usually only one fetus, may be twisted or rotated. In unipara, because of the strong intercornual ligament and the distention of the uterine horns and body with placenta and fluid, both gravid and nongravid horns are in-

volved in the torsion. Torsion involving both horns of the uterus cannot occur in the bitch and queen.²

Torsion of the uterus is most commonly observed in dairy cows and is occasionally seen in beef cows, bitches, queens, ewes, does and mares and rarely seen in the sow.^{4,15} Two rare cases of torsion of both uterine horns in sows were reported.¹⁵ Uterine torsion was reported to be more common in draft mares than in light mares.¹ The incidence of uterine torsion in dairy cattle was 7.3 percent in 1555 dystocia cases treated over a 10-year period in the Ambulatory Clinic of the New York State Veterinary College. The incidence of uterine torsion may vary from 1 to 3 percent in Australia to 18 to 25 percent of referred cases in England, Germany and Switzerland.^{5b,10} Uterine torsion is rare in the *Bos indicus* type of cattle.

The possible causes for torsion of the uterus in the cow are many. The lesser curvature of the uterus in advanced pregnancy is supported dorsal laterally by the mesometrium. The greater curvature lies free in the abdominal cavity resting on the abdominal floor and supported by the rumen, the viscera, and the abdominal walls. The ovarian end of the gravid horn of the bovine uterus is a relatively small or narrow base upon which the uterus rests. If the nongravid horn is small or nonfunctional the instability of the uterus is increased. This anatomical arrangement, together with the manner in which the cow lies down, with the fore quarters going down first, and rises, by elevating the rear quarters first, so that each time the cow lies down or rises the gravid uterus is suspended in the abdominal cavity, means that a sudden slip or fall in either lying down or rising could cause torsion. Other factors aiding torsion of the uterus in advanced pregnancy are lack of fetal fluids, and violence such as sudden falls or rolling. In bitches and queens this latter factor is probably important. Confinement in stables for long periods favors torsion in the cow. The incidence of torsion as a cause of dystocia in pastured cattle was 2.7 percent and in stabled cattle 8.6 percent.¹⁶ In the experience of many veterinarians in New York State most of the cases of uterine torsion occur during the early spring months after cows have been stabled for 4 to 6 months. Torsion is observed more commonly in pluriparous than in primiparous animals. A lack of tone of the pregnant uterus—a condition composed of a lack of fluids, flaccid uterine walls, a small nongravid horn, a long flaccid mesometrium—favors uterine torsion. A deep capacious abdomen predisposes to uterine torsion. Twins in ruminants tend to prevent torsion by making a broader base for the uterus to rest upon and by filling the abdominal cavity. However, 5 of 10 cases of uterine torsion in ewes were in bicomual twin pregnancies^{5b} even though the ovine

mesometrial attachment is sublumbar as in mares.¹ In some cases strong movements of the fetus in the early stages of parturition probably can cause uterine torsion.

Uterine torsion is observed most commonly in advanced pregnancy. However, cases of uterine torsion in the cow have been observed from 70 days of gestation to term. Torsions occurring before the seventh month of pregnancy in the cow are unusual. Several cases in cows¹⁶ and queens¹² have been recorded in which uterine torsion occurred in nonpregnant uteri containing purulent exudate. Most bovine torsions occurred during the early part of the second stage of labor or the latter part of the first stage.¹ This conclusion was based on observations that the cervix is found to be dilated immediately after the torsion is relieved in most of the bovine dystocia cases due to torsion of the uterus. In only occasional cases is there a severe edema due to venous congestion or other circulatory disturbance in the uterus or its contents. In cases diagnosed early the fetus may still be alive. Uterine torsion at this time may be favored by unequal contractions of the uterus or by active movements of the large bovine fetuses.¹ These movements are greatest during the first stage and early second stage of parturition. One mare developed uterine torsion immediately after a period of intense fetal activity.⁸ Probably other factors may be involved in the torsion, as it appears difficult for either uterine contractions or fetal activity alone to produce torsion.

Uterine torsions of cattle of 180° may occasionally be present for days or weeks without clinical symptoms until labor begins and dystocia results. In these cases¹⁶ and the occasional similar cases observed by the author, no evidence of circulatory interference was present. If circulatory interference of the blood supply to the uterus was present, acute clinical symptoms and death of the fetus would probably occur. During pregnancy 45° to 90° torsions or rotations of the uterus are rather frequently found on rectal examination. These often appear to correct themselves before or at parturition.

For the above reasons this writer believes that some cases of bovine uterine torsion of 90 to 180° occur during the last few months of gestation, persist for days, weeks or months and only become evident at the time of parturition. In unusual instances torsion of the uterus may involve a 360° or more rotation of the uterus. One author cited a case involving two complete turns.¹⁶ In torsions of greater than 180° to 240° the birth canal at parturition is usually tightly closed, so that the cervix and the fetus are not palpable per vagina. These severe torsions may cause obstruction of the blood supply to the uterus, with resulting congestion, edema, shock, death of the fetus, and even gangrene of the uterus. In neglected cases

transverse rupture of the uterus or vagina, emphysema and maceration of the fetus, shock, collapse, and death may occur. In rare cases one of the large uterine vessels may rupture, followed by severe hemorrhage into the abdominal cavity. In the bitch transverse rupture of the twisted segment of the uterus often occurs at parturition when the uterus contracts and the fetuses are released into the abdominal cavity. Rarely uterine torsion may be associated with mummification of the fetus late in gestation, instead of emphysema and maceration.

In torsion in cows, ewes and does the cephalic portion of the vagina is usually twisted. Occasionally in a uterus lacking fluid or tone the torsion may occur cephalad to the cervix and in severe torsions at the time of parturition the twist may actually involve the cervix. In multiparous animals, since there is no intercornual ligament, usually one entire horn rotates at the point of its junction with the body and the other horn. Occasionally only a portion of the horn is involved, the twisted portion may occur anywhere throughout the horn. In rare cases in multipara in which both uterine horns are involved in the torsion, the cranial portion of the vagina is twisted. There are a number of reports in the literature on multipara in which the twisted portion of the horn or the entire horn with its fetuses separated completely from the body of the uterus during pregnancy. The fetuses may rupture from this blind sac into the abdominal cavity at the time of parturition, or this separated portion of the horn may be walled off as a passive body in which the fetus or fetuses may macerate or mummify.

Torsions in uniparous animals are either torsions to the right (clockwise) or to the left (counter-clockwise). Most authors agree that left torsion occurs more often than right.^{1,5b,10} If the right horn is gravid the torsion is apt to be to the right.¹⁰

The signs, prognosis, and handling of torsions causing dystocia at the time of parturition will be discussed later. The following paragraphs will deal with the symptoms and prognosis of severe torsions during the gestation period that may be recognized prior to parturition. Although treatment of these antenatal torsions will be mentioned at this time they are similar for torsions resulting in dystocia and so will be discussed in detail in Chapter 10.

The symptoms of torsions of the uterus in the cow prior to parturition may be completely lacking if the torsion is of a mild degree, 45° to 90° or even 180°. When the torsion is 180 degrees or more, definite signs of abdominal pain usually may be noted, such as anorexia, constipation, lack of ruminations, weak and slow rumen contractions, rapid pulse rate, restlessness or colicky symptoms, treading, and tail switching. These symp-

toms may be confused with traumatic gastritis, indigestion, pyelonephritis, or intestinal intussusception. Uterine torsion during pregnancy in the ewe is characterized by a stiff, stilted gait and a stretched, "sawhorse" attitude resembling signs of peritonitis and intussusception or volvulus.⁶ Whenever any cow over six months pregnant shows these suggestive symptoms, a rectal examination should always be made to determine if torsion of the uterus is present. In right torsion the right broad ligament is pulled strongly downward and under the twisted uterine body or vagina, and the left broad ligament is pulled tightly across over the top of the cervix, the body of the uterus, and the vagina, toward the right side. In counter-clockwise, or left torsion the location and direction of the two broad ligaments is reversed, with the right broad ligament crossing over the top of the twisted portion of the birth canal (See Chapter X). The uterine arteries on both sides are tightly stretched. The amount of tension on the broad ligaments and arteries will help determine the severity of the torsion. The fetus is often difficult to palpate but the position of the fetus in the uterus in advanced pregnancy may further indicate the degree of torsion. A dorso-pubic position of the fetus usually occurs when the torsion is 180°. A rectal examination is preferred over a vaginal examination because occasionally the twisted portion of the genital tract may lie cephalad to the cervix in the region of the body of the uterus and not extend back into the vagina. In most cases of torsion of the uterus in cows the cephalic portion of the vagina is involved, the vaginal walls are spirally twisted and a stenosis of the vagina is present. Starting from the dorsum of the vagina, if the folds spiral forward and downward to the left, or counterclockwise left torsion is present; and if the folds spiral downward and forward to the right or clockwise it is a right torsion of the uterus. Rarely torsion may be suspected on external examination of the vulva by the dorsal commissure being pulled forward to the left or right. This is more noticeable in advanced pregnancy when the vulva is relaxed and edematous. In severe cases of torsion occurring in late pregnancy the blood supply to and from the uterus is severely restricted or cut off. In these cases marked symptoms of complete anorexia and constipation, fetid diarrhea, complete lack of ruminations and rumen activity, very rapid and weak pulse, rapid respirations, expiratory grunt, normal to subnormal body temperature, cold extremities, shock, collapse, and death may occur within 24 to 72 hours. In other cases the fetus may die, become emphysematous and macerate or rarely become mummified and the cow develop only slight or mild symptoms. A rectal examination may reveal chronic adhesions, perimetritis, or even an extrauterine fetus if

the uterus has ruptured. This latter condition usually occurs at the time of parturition. In ewes symptoms are similar to those in cows. In multipara, symptoms of abdominal involvement in advanced pregnancy should always cause suspicion of torsion of the uterus. An exploratory laparotomy in ewes and multipara is often indicated.

In a review^{5a} of uterine torsions in mares, most cases occurred from 8 months of gestation to term, average 9 months, with torsions of 180 to 360 degrees. Unlike torsion in the cow, uterine torsion in the mare rarely involves the cervix and vagina. Thus vaginal examination as an aid to the diagnosis of equine uterine torsion is seldom of value. In the cow over 90 percent of uterine torsions are recognized at term while in the mare nearly all uterine torsions are recognized late in gestation with very few mares being in labor when the torsion is diagnosed. All pregnant mares exhibiting signs of colic in the last trimester of gestation should be examined rectally for evidence of uterine torsion as revealed by the location and tension on the twisted broad ligaments and a narrowing of the lumen of the small colon. In the mare torsions to the left or right are reported with near equal frequency.^{5a} If possible the fetus should be palpated to determine if it is alive or dead. Also if mares show severe colic, uterine rupture or incarceration of a portion of the intestine in the torsion may have occurred. The method preferred by some veterinarians of correcting uterine torsion in the mare is the standing laparotomy operation in the flank region on the same side as the direction of the torsion. The alternate lifting and pushing or rocking of the uterus by grasping the fetal limbs through the uterine wall greatly facilitates the correct replacement of the uterus. By this procedure over 50 percent of the fetuses and 70 percent of the mares survived.^{5a} This is possibly a higher recovery rate than the simpler Schaeffer technique of rolling the mare under sedation or anesthesia preferred by the author. If complications are present, alternate surgical approaches should be considered.

The prognosis in torsion of the uterus prior to parturition depends upon the degree of torsion, the severity of symptoms, and the length of time it has existed. In mild cases without symptoms—found by accident on rectal examination—in which the torsion is occasionally 180° but usually 90° or less, the prognosis is good, since the torsion seldom worsens, and treatment is often not necessary. In 180° to 270° torsions causing definite symptoms that are diagnosed and treated early, the immediate prognosis is usually good for the dam and fetus, but the torsion may occasionally recur prior to parturition. In advanced, severe, and neglected cases the prog-

nosis is poor for the life and reproductive life of the dam and usually the fetus is dead.

Depending upon the circumstances the two treatments most apt to be successful in antenatal cases of 180° to 270° torsions in which the condition is diagnosed promptly are: rolling of the cow or mare by Schaeffer's method described by Arthur^{2,7} or correcting the torsion manually by means of a laparotomy. This latter technique was highly satisfactory by a flank approach in either the recumbent or standing mare.^{5a,9,13,14} These authors reported that 5 of 10 mares in which torsion of the uterus was corrected by rolling died;^{3,14} this technique was apparently more dangerous than a laparotomy. The author and others have successfully corrected uterine torsion in mares by rolling.^{3b} Attempts at correcting torsion by manipulation through the rectum or vagina or both in cows in which the cervix is sealed are usually not successful. Hoisting the rear parts of the cow to effect reduction of the torsion is crude and unnecessary, but may be effective in the ewe.¹ In rare cases cesarean section may be indicated when pregnancy is near term. Extrauterine fetuses, fetal maceration, or mummification associated with torsion are handled as described previously.

In advanced severe cases in which gangrene of the uterus is present, laparohysterectomy is indicated in the bitch and queen but is usually unsuccessful in the cow. Further detailed description of the handling of uterine torsions is discussed in Chapter 10 under handling of torsions causing dystocia.

Vagino-cervical Prolapse

Prolapse of the vagina usually involves a prolapse of the floor, the lateral walls and a portion of the roof of the vagina through the vulva with the cervix and uterus moving caudad. Not infrequently the entire vagina and cervix are prolapsed through the vulva. Vagino-cervical prolapse is seen in all species of domestic animals but most commonly in the cow, especially Herefords and Santa Gertrudis and the ewe. The incidence of ovine vaginal prolapse was reported to be about 0.5 percent but in some flocks this may reach 20 percent.¹⁶ In dairy cattle it is observed most often in the larger dairy breeds such as Holstein and Brown Swiss. In young, brachycephalic dogs prolapse of the vagina at the time of estrum is fairly common. It is practically unknown in cats.⁴

The causes of prolapse of the vagina and cervix are probably multiple. It is observed in the cow most commonly the last 2 to 3 months of gestation when a large amount of estrogenic hormone is being secreted by the placenta. This causes a relaxation of the pelvic ligaments

and adjacent structures and an edema and relaxation of the vulva and vulvar sphincter muscles. When the cow lies down the intra-abdominal pressure especially in late pregnancy is transmitted to the flaccid pelvic structures tending to force the relaxed and loosely attached vaginal floor and walls through the vulva. The vesico-genital pouch is the least restraining part of the pelvic structures and when subjected to increased abdominal pressure the bladder and other viscera are forced against the most yielding part—the floor of the vagina.¹¹ Why this condition affects certain cows and not others is not known but it can be theorized that certain cows produce more estrogens and develop a greater relaxation of the pelvic structures earlier in pregnancy. Conformation may favor prolapse. Prolapse of the vagina may be influenced or due to hereditary or genetic factors in Hereford cattle and sheep and Boxers and Bulldogs.^{4,16,29,38} Since prolapse of the vagina is observed more commonly in pluripara than primipara, injuries or trauma of the caudal vagina and vulva at the first or subsequent parturitions may predispose to prolapse during later gestation periods. This is probably a very common predisposing cause in older cattle especially if they were immature or poorly grown heifers and required great traction to relieve dystocia occurring at the first parturition. The condition is favored by close confinement especially in stanchions in which the cow's rear parts project over the gutter and in sheep, especially those confined on lush pastures and carrying twins.^{1,2} It is seen less commonly in pastured cattle. Overdistention of the abdomen or excessive amounts of loose pelvic fat favor the condition by increasing the intrapelvic pressure. These factors are not important unless the pelvic and vulva structures are relaxed enough to allow the vaginal wall to prolapse. An hereditary cause is suspected occasionally in cattle if a dam and her daughter both develop vaginal prolapse. The high incidence of this condition in Hereford cattle may indicate a possible hereditary factor in this breed.

This condition is occasionally observed in dairy cattle following parturition. At this time it is often associated with cystic ovaries, another condition characterized by excessive estrogen production.

In dogs, especially noted in Boxers and the larger breeds, most cases of vaginal prolapse occur during proestrus and estrus and regress during metestrus, only to recur again at the next estrus. Protrusion of the hypertrophied vaginal mucosa or prolapse may occur. The latter is usually due to heredity, excessive estrogens and their relaxing effect on pelvic and perineal structures, tenesmus, forcible separation of the male before the end of coitus and disproportion in size between the two sexes. In a few instances the ration may play a role in the cause

of this condition. In swine and occasionally cattle the feeding of moldy corn or barley containing an estrogenic mycotoxin, may cause edema of the vulva, relaxation of pelvic ligaments, tenesmus, and prolapse of the vagina and even the rectum. Young swine and cattle are more often affected.^{17,20} This condition has been called vulvovaginitis and is generally considered to be due to a high estrogen content in the moldy feed.²¹ Certain types of legumes such as subterranean clover in Australia may contain a high level of estrogens and produce permanent sterility in ewes due to cystic degeneration of the endometrium, marked mammary growth and development, great enlargement of the bulbo-urethral glands in wethers, uterine inertia and dystocia, as well as a high incidence, 10 to 12 percent, of prolapse of the vagina in nonpregnant ewes.³ The development of vaginal prolapse ceased after removing the ewes from the subterranean clover pastures.²⁸ Proper fertilization and rotation of pastures to maintain a certain percentage of grasses largely prevented this condition in sheep pastured on this type of clover.⁷ The former use of stilbestrol or estrogens in fattening lambs in the United States produced vaginal prolapse.⁸

Once prolapse of the vagina or cervix has occurred the exposed mucous membranes as well as the vulvar and vestibular mucosa become very edematous, inflamed, irritated, infected, and occasionally necrotic. The bladder may prolapse through the vulva within the vaginal floor and continue to fill with urine. These factors tend to prevent the return of the prolapsed structures when the cow rises, and favor tenesmus, or straining, that may lead to prolapse of the cervix and the rectum and to exhaustion. In most cases occurring during the late gestation period, the symptoms usually cease after parturition. There is no relationship between prolapse of the vagina and cervix prior to parturition and prolapse of the uterus after parturition. Prolapse of the uterus is no more likely to occur when prolapse of the vagina has preceded parturition than in cows not affected. Prolapse of the vagina and cervix will invariably recur and become more severe during subsequent pregnancies.

The symptoms of vagino-cervical prolapse are obvious and the condition is often spoken of by the farmer as "casting of the wethers." In the cow this condition is usually observed the last 2 to 3 months of gestation with an increasing incidence as parturition is approached. Occasionally it is seen as early as 4 to 5 months of gestation. In a few cases it is observed after parturition in the cow. In the ewe and other species of domestic animals it seldom occurs other than a few weeks prior to parturition except in the dog. Prolapse of the vagina in the bitch is seen most commonly at the time of estrus. The



Figure 82. Prolapse of the vagina in a first-calf heifer.

symptoms may vary from a mild protrusion of the vaginal mucous membrane through the vulvar lips when the cow lies down, to a severe necrotic vagino-cervical prolapse containing a greatly distended bladder and complicated by a prolapse of the rectum due to the constant tenesmus (see Figures 82, 83, 84). In mild cases the prolapsed vaginal wall returns to its proper position when the cow rises. The degree of vulvitis, vaginitis, and cervicitis will vary depending upon the length of time the condition has existed and the type of mechanical, thermal, or infectious agents acting upon the prolapsed mucous membranes. The symptom of straining or tenesmus may be absent, intermittent and mild, or severe and nearly constant, depending upon the degree of the prolapse, the degree of inflammation, edema and irritation involving the genital canal, and the degree of distention of the bladder. Edema of the prolapsed vagina and cervix occurs because of the irritation and trauma to the exposed mucous membrane, and because this portion drops over the ischial arch thereby causing a passive venous congestion. This edema tends to accumulate in the submucosa and cause a separation of the mucosa from the under-



Figure 83. Prolapse of the vagina, including the bladder, in a cow.

lying thin muscular vaginal wall. The cervical seal usually remains intact; although if the cervix is prolapsed and inflamed, the external portion of the seal may be absent. Occasionally the cervix relaxes, the cervical seal is lost and abortion or premature parturition occurs within 24 to 72 hours. If breeding records are not available, a rectal or vaginal examination should be made to see if the fetus is still alive and to determine the approximate stage of gestation. These factors are important in the prognosis and treatment. If the fetus is alive, the uterine artery has its characteristic "whirr," or fremitus, and the fetus moves when its foot or eyeballs are pinched or its leg or jaw is pulled. In some recently purchased cows vulvar scars may be found indicating previous treatments for vaginal prolapse during other pregnancies. In ne-

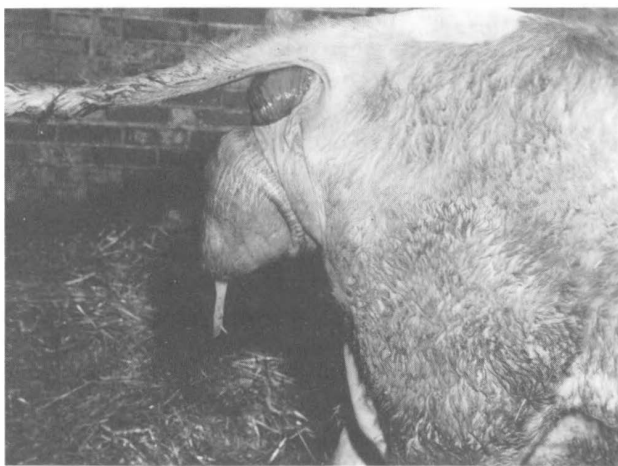


Figure 84. Prolapse of the vagina and cervix with a secondary prolapse of the rectum in a cow.

glected, severe cases the exposed mucous membrane may be necrotic resulting in a toxemia and septicemia. This together with exhaustion caused by the constant straining may cause a fast, weak pulse, anorexia, rapid loss of weight, general body weakness, death of the fetus, possible uterine infection and death. Necrosis or gangrene may even involve the cervix and the caudal portion of the uterus secondary vascular insult and thrombosis. If prolapse of the vagina occurs postpartum, the ovaries should always be examined for the presence of cysts and if no cysts are present the vulva should be examined for injuries. In the ewe suffering from prolapse of the vagina or cervix, death and maceration of the fetus followed by the death of the dam is not uncommon. Severe infections of the birth canal associated with prolapse of the vagina may result in uterine infections or retained afterbirth following parturition or abortion. Differential diagnosis should rather easily distinguish between prolapse of the vagina and cervix, and cystic Bartholin's glands, hematomas of the vulva, tumors of the vagina or vulva, prolapse or eversion of the bladder, rupture of the vagina and prolapse of perivaginal fat, and thick heavy fetal membranes. Cows will usually calve without assistance in nearly all uncomplicated cases. After parturition the prolapse is usually immediately relieved.

The prognosis in prolapse of the vagina and cervix depends upon the severity of the condition and the length of time it has existed. Except in extreme or severe cases, the prognosis is generally fair to good for the life of the animal and the fetus if treatment is prompt and aftercare is good. The condition will recur at subsequent gestation periods unless suitable procedures are followed to prevent it. In the more extreme conditions complicated by prolapse of the rectum, death of the fetus, impending abortion, septic metritis, severe necrosis of the prolapsed organs, exhaustion, septicemia and toxemia, marked debility of the patient, or constant and violent straining, the prognosis is guarded to poor. Slaughter should be considered after parturition or weaning of the newborn because of the tendency for this condition to recur and the possible hereditary nature of the condition. In sheep the prognosis is more guarded, since 10 to 20 percent of pregnant ewes may die or expel dead fetuses.

The method of treatment selected for handling prolapse of the vagina and cervix will vary with the species and breed of animal, the severity of the condition, the stage of pregnancy and the ability of the owner to care for and observe the animal until after parturition. Early prompt treatment often permits the use of simple conservative methods and obviates the necessity of using more heroic techniques. Many methods of handling prolapse of the vagina are available. These will be discussed

in order from the conservative to the more heroic methods used in cattle and then the handling of prolapse in the other species will be mentioned. The operator should select the most conservative method possible under the circumstances and caution the owner that as pregnancy progresses other methods may need to be used to control the condition. Combinations of methods may be used.

Of the 16 procedures or techniques described in the second edition (1971) to correct prolapse of the vagina and control straining or tenesmus, 4 have been eliminated in this third edition because they have not been generally accepted by practicing veterinarians even though some beneficial effects were originally ascribed to them. They are: (1) the use of progesterone injections to control vaginal prolapse in mild or early cases,³⁷ (2) the technique for removal of large deposits of perivaginal fat;^{12,13} (3) the use of artificial pneumoperitoneum to control tenesmus,^{10,31} and (4) the technique of unilateral pudendal neurectomy.^{9,33} Although the vaginal reefing operation for chronic vaginal prolapse¹¹ may only occasionally be used, the author has briefly described it because it may be of value in chronic vaginal hypertrophy and prolapse in bitches.

(1) In mild cases in cattle in which only a slight prolapse occurs when the cows lie down, the cow should be removed from the stanchion and placed in a box stall. In slightly more advanced cases (2) one may elevate the rear parts of the cow in a stanchion by means of an inclined platform that raises the rear quarters 2 to 6 inches higher than the front quarters. In a stall this may be done by building up the bedding under the rear quarters or digging out the soil under the front quarters. This practice has been frequently followed in many of the mild cases of prolapse without any untoward effects with the exception that the rear quarters of the dairy cow have been difficult to keep clean. This simple procedure has prevented many mild cases from becoming more severe and has circumvented the use of trusses or vulvar sutures. It is most practical in dairy cattle.

In replacing the prolapsed bovine vagina and cervix epidural anesthesia using 5 to 8 ml. of 2 percent procaine or xylocaine solution is very helpful and usually necessary particularly in the more severe cases where tenesmus is present. Blocking the internal pudendal nerves in cows, in the manner described for bulls,¹⁹ anesthetizes the vulva and vestibular structures without affecting any motor nerves which is often observed in epidural anesthesia. It is advisable to have the animal standing, preferably with the rear parts elevated to facilitate replacement of the prolapsed organs. In smaller animals the lifting or even suspending of the rear parts off the ground is easily accomplished and greatly aids replacement. The

prolapsed portions should be washed free of dirt and debris with a mild, nonirritating antiseptic solution or physiological saline. If irritation, infection, or straining is present a bland antiseptic oil, or sulfonamides or antibiotics in oil or ointment, might be of value when applied to the prolapsed vagina before replacing, and injected into the vagina once to twice daily for several days or more after replacement. If difficulty is encountered in replacement of the prolapsed vagina with the distended bladder inside it, the prolapsed portion may be raised dorsally to reduce the sharp kink in the urethra, thus permitting the urine to escape. In exceptional cases it may be necessary to trocarize the bladder through the prolapsed vagina wall with a large-gauge needle. Once the vaginal floor and walls are replaced the normal circulation is restored and the edema in the vaginal walls and mucous membrane is rapidly reduced. If the vagina is badly infected the animal may have an elevated body temperature. In these cases or those in which the cervix is relaxed and dilated and abortion appears likely, a course of antibiotic or sulfonamide therapy is indicated to control infection and septicemia, and if abortion does occur to prevent septic metritis.

(3) The vulvar truss is of practical value in controlling prolapse of the vagina in dairy cattle confined in stanchions or box stalls where the owner is able to check and adjust the truss as needed. These trusses may be made of rope, leather, or metal. An aluminum rod truss²⁶ held in place with ropes is easily molded to fit the individual cow. These trusses are held in place by ropes or leather straps securely fastened to a surcingle around the cow's chest and neck. The truss, as it fits over the vulva, may be padded with toweling or burlap to prevent abrasions or necrosis where it lies against the ischial arch. When the cow arches her back to urinate or calve the truss will loosen. Cows have been reported to have calved with the truss in place. Many dairy farmers prefer these simpler, less drastic methods, 1 through 3, for handling vaginal prolapse. Most cases are mild and when treated early the results are satisfactory. The above techniques are not usually satisfactory when tenesmus is severe or vagino-cervical prolapse is marked.

(4) Pessaries which are popular in Europe consist of a long narrow wine bottle or similar blunt round object inserted into the vagina after replacement. Pessaries are held in place by a narrow piece of wood or metal placed into the bottle with a ring or loop on the end projecting out of the vulva. A rope is fastened through this ring similar to ropes that hold a metal, plastic or leather truss in place. A light metal rod or plastic pessary shaped like a hairpin with long lateral arms containing eyes so it could be fastened to the wool of ewes has been described and

is available commercially in the United States.¹⁶ Pessaries have not been popular in the United States because an object placed in the vagina tends to cause straining and expulsion of the pessary.

(5) Vulvar sutures that do not pass through the vulvar lips are often a satisfactory method of treating vaginal prolapse for a limited period especially the last 2 to 3 weeks of gestation. The sutures should be located at least 2 to 3 inches lateral to the vulvar lips in the hair line. This affords a much tougher and thicker skin for the suture, which does not tear out as readily nor cause as much irritation as one in the vulvar lips. It is desirable to use a type of suture that can be untied or released, so that if a cow appears to be near or in the first stage of parturition the vulvar sutures can be unfastened, so that calving can occur. If the calving time has been misjudged and prolapse again results, the prolapsed vagina may be washed and replaced. If prolapse does not occur, the sutures can be retied. This is not possible with the simple horizontal figure-eight or horizontal mattress sutures that do not pass through the vulvar lips or deep horizontal mattress sutures, usually of double thickness one-eighth to one-quarter-inch thick umbilical tape, that have been passed through each lateral wall of the vulvar vestibule and including the vulvar lips. Another advantage of the type of suture that can be untied is that if there is some possibility of postpartum prolapse of the vagina, or even the uterus, the sutures can be retied after parturition and left for several more days. Although some suppuration occurs around these stitches they may be left in place for as long as 6 to 8 weeks. The vulva-suturing technique preferred by the author is one employing 4 to 5 small separate loops of doubled 1/4-3/8 inch umbilical tape or heavy nylon on either side of the vulva in the hair line from the level of the anus to about opposite the lower commissure of the vulva.¹² About 2 feet of 1-1/2-inch to 3-inch gauze bandage, doubled, is used to lace up the loops in a manner similar to lacing a shoe. This gauze may be removed or replaced as desired. A similar but crude technique is the use of hog rings instead of umbilical tape loops. These tend to tear out or work out of the skin. A metal skewer type of needle with large wooden buttons to hold the vulvar lips together and other metallic clamp-like devices have been advocated by European veterinarians and are available commercially. Some veterinarians prefer quill, button, or deep horizontal mattress sutures of umbilical tape, through the vulvar skin, muscle, and mucous membrane.^{18,32}

(6) A buried or "hidden" purse-string type of suture, Buhner's method, for the vulva following replacement of a prolapsed vagina has been described.^{1,6,27} This technique may be used in chronic postpartum prolapse as

well as prepartum prolapse. Under epidural anesthesia and with a near-sterile procedure, two one-half inch incisions are made one to two inches above the upper commissure and below the lower commissure of the vulva, respectively. With a long eye-point needle similar to a seton needle, an 18-inch piece of one-eighth inch thick nylon cord, heavy "Vetafil" or nylon sashcord is passed within the tissues from one incision to the other near the hairline lateral to one vulvar lip. The needle is withdrawn and reinserted in the opposite direction lateral to the opposite vulvar lip to the lower incision site and again withdrawn. The purse-string suture around the vulva is tightened sufficiently to allow 4 fingers in the vulva, and a bow knot is tied with long ends. Thus, the farmer may loosen this suture if parturition is imminent and if necessary tighten and retie the suture after calving.

(7) A vulva-closing technique modified from the Caslick operation in mares has been of great assistance in the treatment of chronic prolapse of the vagina 2 months or more before parturition or in postpartum prolapse in cows. It has also proved very valuable in controlling tenesmus associated with "windsucking" and a highly inflamed vaginal and vulvar mucous membrane. The drawing of air into and forcing it out of a highly inflamed vagina appears to stimulate and produce violent straining. This operation is performed under epidural anesthesia. After replacement of the prolapsed structures, the caudal 3/4 inch of mucous membrane of both vulvar lips from and including the superior commissure to about 1-1/2 inches above the ventral commissure is removed with scissors. These raw areas of both vulvar lips are sewn together with interrupted vertical mattress sutures of fine catgut, nylon or silk suture closely spaced. One or two deep horizontal mattress vulvar sutures of umbilical tape are placed through the skin 2 or 3 inches lateral to the vulva and through the vulvar muscles and mucous membrane to prevent the vaginal wall being forced against the fine sutures in the vulvar lips and thus tearing them out if tenesmus occurs (see Figure 85). After 10 days all sutures may be removed. The vulvar opening is then so small that the vaginal wall cannot prolapse and air cannot gain admittance to the vaginal lumen. Just before or at the time of calving it is necessary to slit this adhesion between the vulvar lips to prevent its tearing out. Because of the tendency to repeated prolapse at each gestation period, resuturing is advised immediately after calving if artificial insemination is employed or after breeding if natural service is used.

(8) Minchev's method^{14,23} for controlling prolapse of the vagina by surgically fastening the cranial portion of the vaginal wall through the dorsolateral wall of the sacroscopic ligament, muscles and skin of the croup was

slightly modified⁵ to place the stay sutures dorso-cranial to the lesser sciatic foramen.^{14,15,25} After replacement of the prolapsed vagina under epidural anesthesia the anterior portion of the vagina is fastened to either side of the pelvic cavity preventing a prolapse by means of anchoring devices including gauze rolls, heavy plastic buttons, large overcoat buttons or 3/16th inch thick pads of industrial belting. In securing the vaginal walls to the pelvic walls with these anchors inside the vagina and outside on the skin of the croup, heavy suture material such as 1/4 or 3/8 inch umbilical tape doubled or heavy Vetafil or nylon cord so that if straining does occur the vaginal wall will not be lacerated freeing it from its attachment to the pelvic wall. The sutures fastening the vaginal and skin buttons together may be inserted under local anesthesia by making small incisions in the skin of the croup over the sacroscopic ligament and inserting a small rumen trocar or a crochet-type hook into the vaginal cavity to guide or carry the suture material fastened to the vaginal button to the outside button on the skin. One may also do this by carrying a 4 to 6 inch needle threaded on the suture material attached to the vaginal button into the vagina and forcing the needle dorsolaterally through the skin. In inserting the needle or trocar care should be taken to avoid the rectum, the pudendal nerve and vessels and the sciatic nerve that can be palpated medial to the sacroscopic ligament. The authors originally describing this technique recommended that the sutures be removed in 10 to 14 days at which time the vaginal wall was firmly adhered to the pelvic wall. Firm attachment frequently does not occur by this time and prolapse of the vagina may again recur. For this reason many veterinarians leave the buttons and sutures in place until after calving.

(9) Another recently introduced technique (Winkler) for handling prolapse of the vagina is fixation of the cervix to the prepubic tendon, cervixepxy.^{24,36} This procedure minimized tenesmus, required no aftercase during gestation or at parturition, prevented recurrent prolapse at subsequent pregnancies and could be used in all types of cases. Under epidural anesthesia the prolapsed vagina is carefully cleaned and replaced. A 3 or 4-inch half circle cutting edge suture needle is bent into a U-shape and threaded with 36 to 48 inches of heavy 3 or 4 nylon or "Vetafil," noncapillary suture material. Material such as umbilical tape should not be used. The needle and suture material are carried into the vagina. The bladder is pushed laterally away from the midline. The needle is passed through the floor of the vagina beneath the external os of the cervix in a lateral to medial direction just cranial to the pubic symphysis and just to the right or left of the prepubic tendon and through a small lateral portion of

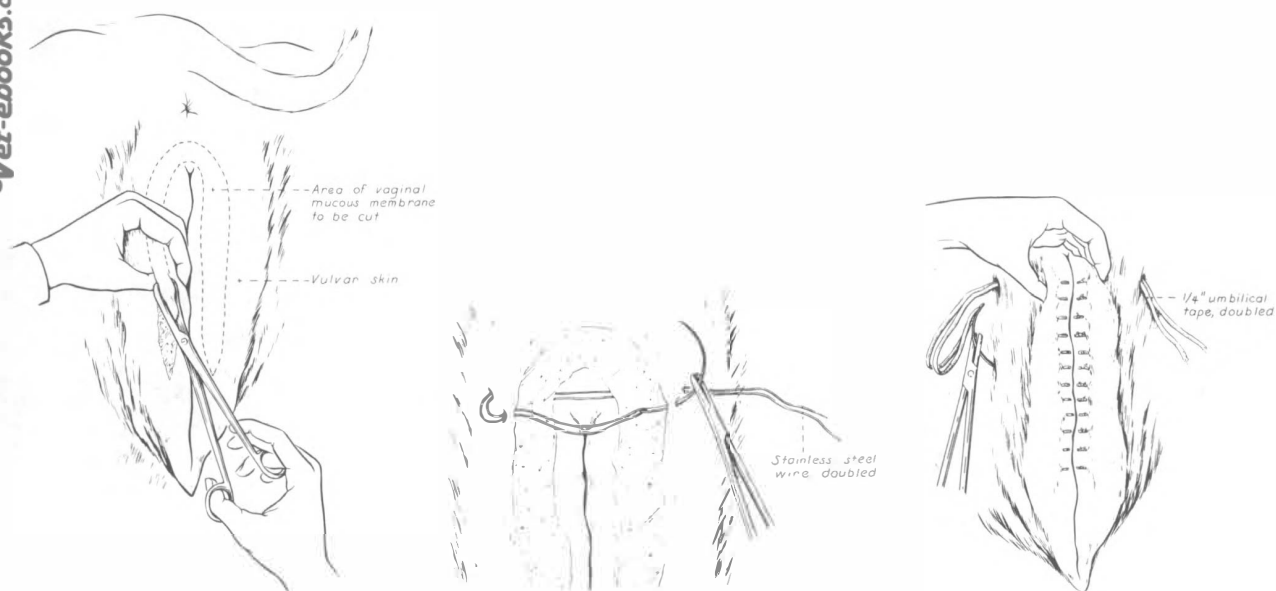


Figure 85. A technique for the control of chronic prolapse of the vagina. (Left) Under epidural or local anesthesia a three-quarter inch strip of mucosa is removed from just inside the vulvar lips. (Center) An interrupted vertical mattress suture is used to draw the wound edges gently together. (Right) If the animal is straining a deep mattress suture is placed through both vulvar lips cranial to the suture line.

the thick prepubic tendon, and then back up through the vaginal floor. This suture should include 1-1/2 to 2 inches of vaginal floor and 1/4 to 3/8 inch of prepubic tendon. The needle is then passed through the ventral half of the cervix at least one-half inch cranial to the external os. The suture is tied outside vulva and the knot carried forward so the cervix is fastened closely to, but not necessarily tightly against, the floor of the pelvis. It may be desirable to pass a catheter into the bladder to make certain it was not included in the suture. These latter two operations (10 and 11) avoid placing sutures in the region of the vulva which is richly supplied with sensory nerves and thus tenesmus is minimized. The suture is left in place indefinitely as it does not interfere with breeding or calving. This operation is performed most easily several months after calving when the uterus has involuted. Cervopexy through a laparotomy in the left paralumbar area may facilitate placing the fixation suture.²⁴

(10) Another surgical "reefing" technique for correction of chronic vagino-cervical prolapse, particularly adapted to selected cases in beef cattle has been described.¹¹ This consists of a submucous resection of the edematous, devitalized mucous membrane from the prolapsed portion of the vagina. If the prolapsed portion of the vagina is large due to the presence of a distended bladder this should not be reduced before the operation as it will make surgery more difficult. Surgery can be

performed under epidural anesthesia. Adrenaline injected or applied locally may aid in reducing hemorrhage during the peeling-off of the diseased, often necrotic, edematous mucous membrane. The sleeve of vaginal mucous membrane that is peeled off is narrow at the dorsum and wide ventrally, as more of the floor of the vagina is usually involved in the prolapse. Incisions on the prolapsed vagina are made in the normal mucous membrane near the cervix caudally and near the urethral orifice or hymen cranially. As the diseased mucous membrane is peeled off, mostly by blunt dissection, No. 3 or 4 chromic catgut suture is used to approximate the two cut edges of normal mucous membrane, as the operation progresses. This is done to control hemorrhage, which is usually quite severe but of a capillary oozing type, and to get most of the incision sewed before the prolapsed vagina begins to drop back into its proper intrapelvic position. In most operations traction applied to the cervix is necessary to keep the vagina retracted and outside the vulva until the suturing is completed. The vagina is greatly shortened by this reefing operation so that the cervix is nearer the vulva. Since the excess vaginal wall is thereby eliminated, the prolapse will not recur during that particular gestation though in rare cases it may during subsequent ones. Tenesmus ceases after the operation. The muscular coat of the vaginal wall is drawn up in folds under the suture line that joins the cephalic and caudal edges of normal vaginal mucous

membrane. In operating on cows in which most of the vagina is prolapsed, care should be exercised in removing the mucous membrane on the dorsal surface of the vagina not to cut too deeply and enter the recto-genital pouch of peritoneum, that extends about 5 inches caudad on the dorsal surface of the vagina. Care should also be used to prevent incising the urethral opening or urethra. Obviously this operation should not be performed if the cow is due to calve within 3 to 4 weeks or if abortion appears likely. This is not an operation to select as a last resort in a neglected case, with the patient exhibiting symptoms of toxemia and exhaustion. The type of case indicated for this operative should be selected carefully. The prolapse should have occurred relatively early in the gestation period or be a chronic postpartum prolapse. The cow should be in good condition for the operation. It is particularly indicated in that type of cow, usually beef, in which regular observation and care of the cow is not possible.

In the bitch, no treatment of mild cases of vaginal hyperplasia and prolapse is indicated, as the condition corrects itself after estrum. In breeding dogs the removal of the prolapsed mucous membranes by a reefing technique similar to the one described in the cow gives good results.^{11,22,32} Episiotomy in the dorsal position may be necessary as an aid in resection of the mucous membrane in the dog.¹⁴ In nonbreeding dogs ovariectomy results in a permanent cure.

(11) In chronic prolapse in postpartum cows treatment with a gonadotrophic hormone or GnRH is indicated if cystic ovaries are present.¹² In unusual cases other methods of handling might be indicated such as a cesarean section late in gestation.

If prolapse of the rectum occurs along with prolapse of the vagina the prognosis is more grave and either a purse-string suture to retain the rectum, a reefing operation, or amputation of the rectum might be indicated, along with feeding or administering mild laxatives or large amounts of fluids to prevent constipation. Prompt slaughter of many animals affected with severe prolapse of both vagina and rectum is advisable as persistent tenesmus is common in these animals.

If constant tenesmus after replacement is a problem, repeated use of local epidural anesthesia at one to two hour intervals may be helpful if accompanied by intravaginal infusions of bland, protective antiseptics in oil. In certain beef cattle some veterinarians have injected 3 to 8 ml. of benzyl, ethyl or isopropyl alcohol epidurally that destroys the nerve tissue resulting in anesthesia to the perineum and paralysis of the tail lasting from 2 to 6 months. This technique is not desirable for dairy cattle for sanitary reasons. The old technique of a tracheotomy

operation to prevent straining is rarely, if ever, necessary or recommended. Recently some of the local anesthetics such as benzocaine, nupercaine, and cyclaine have been incorporated into ointment bases. The application of these ointments to the vaginal and vulvar mucous membranes have been recommended to control local surface irritation and the resulting tenesmus. However, the author has not found these local anesthetic ointments very effective.

Paraplegia of Pregnancy

There are numerous causes for paraplegia, or paresis, during pregnancy. Most of these conditions occur in, or are aggravated by, advanced pregnancy, during which period there is very rapid growth of the fetus and an increase in weight of the gravid uterus as well as a progressive relaxation of the pelvic ligaments and an increase in the size and development of the udder. The factors, and several may operate together, that may cause a cow to exhibit paresis in advanced pregnancy are:

Nutritional deficiencies and starvation—A lack of minerals such as phosphorus and calcium may result in debility, pica, bone and joint lesions, and even an increase in incidence of fractures. A lack of trace minerals, principally copper, cobalt, and iron, has been reported as resulting in anemia and debility, which if extreme may cause weakness and inability to rise. In certain areas such as Florida with high molybdenum levels in the soil and forage, chronic diarrhea coupled with a lack of copper, iron, and cobalt favor debility. Lack of vitamin A in the ration may lower resistance and favor uterine infections. Most nutritional deficiencies are multiple, including a lack of minerals, proteins, carbohydrates, and fats. The classic symptoms of severe underfeeding or starvation are debility, cachexia, weakness, and finally inability to rise; and in advanced cases, death of the fetus, and abortion. In certain areas of the country specific deficiency diseases occur commonly and are known by the local veterinarians. In the high-producing dairy cow it is usually desirable to supply additional minerals to the ration as well as offering them free-choice to compensate for the loss of minerals in the milk and the developing large fetus.

Ketosis—Pregnancy disease in ewes due to a lack of carbohydrates is a common cause for debility and paraplegia in ewes and does in advanced pregnancy. Twin or triplet pregnancy is a predisposing factor. Usually the fetuses die and the ewe often succumbs. If the fetuses are aborted promptly the ewe may recover; or treatment administered early in the disease may bring about recovery. Therapy for ketosis consists of glucose intra-

venously, propylene glycol or glycerol orally and glucocorticoids in small doses parenterally. Large doses of glucocorticoids may induce premature parturition or abortion in late pregnancy. In a valuable ewe near term, cesarean section may be indicated. The carbohydrate intake of the rest of the pregnant ewes in the flock should be increased by feeding grain or molasses. Provision for increased exercise may be helpful. This condition may be observed in the cow and bitch prior to parturition.^{2,4,5}

Grass tetany is seen in pregnant cattle on lush pasture, such as wheat pastures, particularly in the fall or early spring. In areas with soil deficient in calcium and magnesium, it may occur at any time of year even in stabled animals. It is apparently due to a lack of calcium causing hypocalcemia and/or magnesium causing hypomagnesemia. Some believe it is associated with the high potassium or high vitamin A levels of the lush, green immature forage. Mineral feed or feeding of good-quality alfalfa or clover hay rich in calcium, magnesium and phosphorus tends to prevent the condition. It is probably best to remove the stock from the lush pasture for a time. The paretic cases usually respond to calcium therapy, or if paresis and nervous symptoms are present both calcium and magnesium therapy are indicated.

Milk fever or parturient paresis may occur just prior to parturition in the high-producing dairy cow, at which time it is called preparturient milk fever or paresis. Most preparturient cases occur during the first stage of parturition, when milk letdown is favored by the action of the oxytocin released at that time. Following treatment, active labor and calving will often follow within 4 to 6 hours. In a few cases preparturient milk fever, or hypomagnesemia due to a sudden drop in blood calcium and/or magnesium may be observed 24 to 72 hours before parturition. Transport stress in cows late in pregnancy may precipitate this condition.⁶

Puerperal tetany, or eclampsia in dogs and rarely cats associated with a hypocalcemia characterized by nervousness, restlessness, whining, and then staggering, stiffness of the legs, and finally collapse with clonic spasms, labored respirations, salivation, and elevation of temperature, may be seen occasionally prior to parturition although it is far more commonly observed the first 2 weeks after parturition.

Dropsy of the fetal membranes and fetus—This may occur from 5 months to term as has been discussed previously and is associated with a great increase in abdominal weight and size and the inability to rise. The increased abdominal weight may lead to injury such as dislocation of the hips.

Joint and tendon injuries, especially to the rear limbs, may render the animal unable to rise. Dislocation of the

hip is common in the cow in advanced pregnancy, especially after slipping on concrete floors or ice in the barnyard. Dislocation or subluxation of the stifle are occasionally observed. Separation of the ligaments of the ilio-sacral articulation is infrequently observed. Sometimes painful lesions of the joints, due to chronic arthritis of the stifle or hip or suppurative lesions of the hock or coffin joint, may cause reluctance to rise; in time, stiffness, myositis, neuritis and weakness and paresis may result with inability to rise.³ Sudden rupture of the prepubic tendon in the mare or rupture of the gastrocnemius tendon, usually secondary to Zenker's muscle degeneration in the cow, may occasionally be causes in these animals of their being unable to rise or rising with difficulty.

Fractures of the rear limbs or spine—Fractures of the femur and pelvis are the most common of those occurring in advanced pregnancy. They may occur when a cow in advanced pregnancy is mounted by another cow. Osteomalacia due to a prolonged mineral deficiency favors fracture. Excessive relaxation of joints and ligaments due to estrogens present in advanced pregnancy may also lead to fractures. Spinal injuries or fractures in the lumbar region with severe posterior paresis, may occasionally occur. If a cow or bull mounts the pregnant animal, the impact of the sternum on the coccygeal and sacral vertebrae may cause a subluxation, dislocation, or fracture of these vertebrae and subsequent posterior weakness and paralysis of the tail.

Septic or infectious processes associated with advanced pregnancy may cause paresis. They may be any of the following: septic metritis of pregnancy with death and maceration of the fetus; rupture of the uterus with severe peritonitis secondary to an emphysematous fetus; traumatic gastritis with diffuse peritonitis; severe torsion of the uterus with gangrene and shock, or death of the fetus and rupture of the uterus; severe pyelonephritis aggravated by advanced pregnancy; or septic mastitis.

Other conditions that may cause paresis or paraplegia in animals at any time may affect the pregnant animal. These are as follows: rupture of a large uterine vessel with hemorrhage, toxic indigestion, diseases of the central nervous system, such as rabies and listeriosis; severe prolonged illness resulting in debility such as: Johnes disease, severe mange or pediculosis, advanced actinomycosis of the jaw, and senility; tumors especially of the brain and spinal cord, such as lymphocytoma; severe septicemic diseases such as: anthrax, blackleg, pasteurellosis, leptospirosis and anaplasmosis; and severe foot lesions.⁶

If an animal is down, struggles to rise, but remains down for a period of time particularly on a hard concrete

floor, decubital injuries, contusions, abrasions, joint muscle, nerve and tendon injuries, and exhaustion are common. These cause progressive soreness, stiffness, awkwardness, and even greater difficulty in rising. Many so-called malingers or "downer" cows^{2,3,6} have arthritis, myositis, neuritis or tendonitis painful and debilitating enough so that they refuse or are unable to rise. These animals might benefit from good nursing, a dirt floor or heavily bedded box stall, and slings to get them up periodically so as to restore movement and circulation to the legs. Occasionally butazolidin or similar drugs to control inflammation and pain are of value. The further handling of these animals in advanced pregnancy depends upon their value for food, their sentimental value, the value of the offspring, the nature and severity of their diseases or injuries, and the owner's ability, means, and interest in nursing these paraplegic, paretic or "downer" animals.

Miscellaneous Accidents of Pregnancy

Hemorrhages of pregnancy—The most common hemorrhage of pregnancy is that associated with hematic mummification of the bovine fetus. This occurs in the utero-chorionic space of a sealed uterus. Slight hemorrhages occur between the maternal and fetal placenta that may be noted on examination of the placenta after parturition. In the cow "uterine sand," occasionally found in the utero-chorionic space, is dried or inspissated granules of serum about 1/64 to 1/16 inch in diameter. Occasionally due to trauma or violence causing rupture of the larger vessels, hemorrhage or large blood clots sufficient to cause death may be found around the vagina or in the broad ligament in the cow or mare in late pregnancy. Mares should not be transported or subject to violent exercise in late pregnancy for this reason. Hemorrhage or bleeding from the genital tract appearing at the vulva during pregnancy is rare in domestic animals. It may be noted in pyelonephritis, in a traumatic injury to the vagina, vulva or bladder or in tumors of the vulva or vagina that bleed readily. In mares recurrent slight bleeding from a ruptured varicose or surface vein in the vagina or hymenal region is common but not serious; it may heal spontaneously or be corrected by cautery or by surgically ligating the lesion. Bleeding usually ceases after parturition. A reddish-brown vulvar exudate containing free blood may be associated with beginning abortion and a dead fetus or a septic metritis of pregnancy with an open cervix. Hemoglobinuria due to leptospirosis and other acute hemolytic diseases may be confused in the pregnant animal with bleeding from the genital tract.

Rupture of the gravid uterus—This may occur either spontaneously due to unknown causes, or secondary to abortion, dystocia, emphysematous fetuses, chronic peritonitis with uterine adhesions, torsion of the uterus, dropsy of the fetal membranes and fetus, and extreme violence and trauma in advanced pregnancy.

Strangulation of the large colon by the gravid uterus—A mare with unexplainable symptoms of digestive distress proved to have, on postmortem examination, a displacement of the large colon beneath the gravid uterus.⁷ Obstruction of the bowel may also occur associated with uterine torsion.

Strangulation of the pregnant uterus by a pedunculated lipoma—A case of a 4-month pregnancy in a cow was cited in which a pedunculated lipoma wrapped around the uterus.¹

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Chapter VI

PARTURITION

Parturition encompasses the various physiological processes involved in the birth of young including the delivery of the fetus and placenta (fetal membranes) and the involution of the uterus. Prior to parturition the dam should have been fed a properly balanced ration in amounts sufficient to provide the necessary carbohydrates, protein, fat, vitamins, minerals, and water so that at the time of parturition she is neither fat nor thin. Most livestock men prefer to feed their animals approaching parturition a light, slightly laxative feed. Under most systems of management the pregnant animal is provided adequate opportunity for exercise. For the last 2 to 3 weeks prior to parturition violence and excessive exercise or work should be avoided. The animals should be segregated from the rest of the herd in clean, sanitary, comfortable, quiet surroundings.

One of the best locations possible for parturition of farm animals is a small pasture free of woods, steep slopes, wet or brush areas. This location is clean and the newborn are not exposed to the common barn or barnyard diseases. The principal disadvantage of such a location is that frequently close observation or supervision of parturition cannot be followed. During periods of adverse cold and wet weather, a dry, relatively warm building or shed supplied with heat is desirable for parturition for all domestic animals. A satisfactory place often used for parturition of the large domestic animals is a clean, well-bedded, roomy, disinfected box stall. Clean, fresh, dry straw, shavings or sawdust are usually available as bedding but are not ideal because they readily contaminate the fetus, membranes and genital tract. A strong, sterilized, rubberized or plastic covering securely anchored over the above bedding material would be highly desirable. Facilities for sanitation and isolation at the time of parturition or abortion are of prime importance in most herds. A reliable birth detection system for animals, other than the time-consuming repeated checking of those near parturition, has not been developed although preliminary studies have been conducted.^{52b}

In swine in which heavy death losses of 20 to 30 percent of the newborn are frequently experienced during parturition and the following 48 to 72 hours, many life-saving innovations have been introduced. The farrowing

pen should have guard rails. The bedding should not be too deep. Farrowing crates are highly desirable. Constant watch should be kept on farrowing sows to prevent them from lying on the newborn pigs. In many cases the newborn pig is removed immediately after birth. After farrowing is completed, the pigs are returned to the sow. To prevent the newborn pigs from becoming chilled, farrowing houses are built singly and small, or larger farrowing houses are artificially heated. The use of heat-lamp-type brooders placed in the corner of the pens not only prevents chilling but provides a safe place for pigs when they are not nursing. In some farrowing houses heating cable is placed in the concrete floor to provide heat for the pigs. The optimum environmental temperature for newborn pigs is 85° to 95° F. This temperature must be maintained for 3 to 6 weeks as piglets are unable to maintain a normal body temperature when the ambient temperature is low. For dogs, the owner should set aside a whelping place or box about two to three feet square with six to eight inch sides for medium-sized dogs. If possible the bitch should be kept in this familiar environment for at least a month before whelping.

It is important that veterinarians be familiar with normal parturition as it occurs in the various domestic animals so that there may be immediate recognition of any pathological symptoms. Assistance or interference with the birth process, occasionally necessary to save the fetus or dam, must be performed at the proper time. The time of parturition is one of the most critical stages in the life of any animal. It is one of the periods of highest death rate in animals. It can be a period in which not only the fetus, but also the dam, may be severely damaged or injured and thus affect its future reproductive and productive efficiency. This period, therefore, is of vital concern to the farmer who has a large economic investment in his animals.

Symptoms of Approaching Parturition

The signs of approaching parturition in domestic animals are somewhat similar but vary in certain important respects. The symptoms are inconstant between individ-

ual animals and between consecutive parturitions. These symptoms therefore do not permit an accurate prediction as to the exact time of parturition in a certain animal but they are useful indications as to the approximate time parturition may be expected. The practicing veterinarian is frequently asked to examine and predict the time of parturition of an animal in advanced pregnancy. Although the following discussion will be helpful in this respect, he should refrain from making too positive or definite a statement concerning the exact time of parturition, as subsequent events will more often than not prove him wrong.

The breeding date, if known, is helpful in predicting the approximate time of parturition. Breeding records are necessary on the well-managed farm. Just prior to parturition most animals tend to segregate themselves from the others. The sow, bitch, and queen attempt to make a suitable bed. Changes in the pelvis, genital organs, and mammary glands take place.

In the cow the pelvic ligaments, especially the sacro-sciatic, become progressively more relaxed, causing a sinking of the croup ligaments and muscles. The caudal border of the sacro-sciatic ligament between the coccygeal vertebrae and ischial tuberosity becomes less cord-like and tight, and more relaxed and flaccid. Relaxation of the pelvic ligaments, cervix and possibly the structures around the perineum is due to edema and changes in the collagen fibers in connective tissue probably caused by an increase in estrogen from the placenta. Relaxin may also play a role. In most cows the presence of very relaxed ligaments indicates that parturition will probably occur in 24 to 48 hours. This relaxation of the ligaments is also noted by the elevation of the tail head. The vulva becomes progressively edematous and more flaccid until it is 2 to 6 times its normal size. The udder becomes enlarged and edematous. In heifers this udder enlargement begins about the fourth month of gestation. In older, pluriparous cows it may not be noticeable until 2 to 4 weeks before parturition. In high-producing, younger cows, the amount of edema in the udder may be extensive and cause difficulty in walking. Edema may extend forward on the abdominal floor to the xiphoid region and be 2 to 6 inches deep. In the region of the navel it may resemble an umbilical hernia. It may extend caudally above the udder and involve the region of the escutcheon and even the vulva. This edema may occasionally be severe enough to interfere with circulation in the skin between the udder and legs or in the region between the fore quarters of the udder, resulting in areas of necrosis at these sites. Just prior to parturition the udder secretion changes from a honey-like dry secretion to a yellow, turbid, opaque cellular secretion called colostrum. At this

period the udder and teats are so distended with colostrum that in "easy milkers" it may leak out. The cow usually exhibits a tenacious, whitish, stringy type of mucus coming from the cranial part of the vagina, starting about 7 months of pregnancy. This mucus becomes more profuse as parturition approaches. Just prior to parturition the amount of mucus increases markedly and the cervical seal liquefies. During the last few hours before calving the cow may exhibit anorexia and restlessness. Heifers may show signs of abdominal discomfort with kicking at the abdomen, treading, raising and switching their tails and lying down and rising. A majority of cows, 67 percent, calve during the night hours.⁹² Other studies indicate that calvings occurred equally between day and night. However, feeding beef cows at night for 1 to 3 weeks before calving altered the calving pattern so 85 percent of 1331 cows calved during the daylight, 6 am to 6 pm, hours when they could more easily be observed.^{60,62b} Further studies are indicated.

In the mare somewhat similar symptoms of approaching parturition are present. The sinking of the sacro-sciatic ligaments is not so pronounced, due to the heavy croup muscles. The vulva does not become as edematous as in the cow but edema and flaccidity are noted the last few weeks of gestation. No discharge of vaginal mucus prior to foaling is noted in the mare. The udder starts to develop noticeably about 3 to 6 weeks before foaling. In most mares the udder and teats become filled and distended with colostrum about 2 days before foaling, and oozing of this colostrum from the teats, called "waxing," is usually observed in 95 percent of mares 6 to 48 hours before foaling. In a few cases no waxing is observed before foaling and in rare cases milk may leak from the teats up to a week or so before parturition. Within 4 hours of parturition slight sweating in flank region and behind the elbows is frequently noticed. Anorexia occurs only within 1 to 2 hours of foaling. As the first stage of labor advances the mare becomes restless, shows slight colicky symptoms, raises and switches her tail and lies down and gets up frequently. These symptoms become progressively more marked until the allantois chorion ruptures and the second stage with actual labor begins.

The mare greatly prefers solitude and quiet at parturition and seems more able than other animals to control or suppress parturition until the night hours, when stable activities are at a minimum. Of 367 foals, 59.8 percent were born from 6:00 p.m. to midnight, 23.4 percent from midnight to 6:00 a.m. and only 16.8 percent from 6:00 a.m. to 6:00 p.m. Thus about 83 percent of the foals were born during the night. Other studies confirmed this percentage of nighttime foalings.^{6,85,99}

In the ewe and goat the conditions are similar to the

cow with the exception that udder development is not so great. **In the sow and queen** the symptoms are somewhat similar to those in the bitch. As pregnancy progresses, **the bitch** becomes quieter and as parturition approaches the vulva becomes flaccid, enlarged, and edematous. The mammary glands also become enlarged and edematous and milk may be present in the udder several days before parturition. The bitch becomes restless and shows anorexia for a few days before parturition. This becomes more noticeable 12 to 24 hours before whelping. During the first stage of labor, the bitch may pant or exhibit an increased respiratory rate. During the latter stages of pregnancy in the ewe, sow, and bitch a mucoid vulvar discharge is usually evident. Environmental disturbances, especially those caused by other dogs, will delay or interrupt the birth process in bitches.¹¹ Seventy-three percent of farrowings occurred between 2:00 pm and 4:00 am.⁵

The Initiation of Parturition

In recent years the exact mechanism concerned with the onset of parturition after a rather regular and definite length of gestation for each species of animals is becoming much better understood. Hormonal factors are of prime importance, as parturition can take place without innervation of the uterus.^{21,33,47,49,60,85}

As described in Chapter IV progesterone from the corpus luteum is necessary throughout gestation in the cow, doe, sow and bitch. Ovariectomy at any stage of gestation in these species results in abortion or premature birth. While in the ewe, queen and mare progesterone from the corpus luteum is necessary to maintain pregnancy only during the early stages of gestation. Ovariectomy may be performed without affecting pregnancy after 55 days of gestation in the ewe, 50 days of gestation in the queen and 70 to 150 days of gestation in the mare. In these latter species, progestogens or progesterone are produced by the feto-placental unit to maintain pregnancy after luteal function ceases.^{21,33}

Estrogen levels, arising from the embryo or fetus and the placenta, are much lower than progesterone levels during pregnancy. In the cow, ewe, sow, doe and queen the estrogen levels rise very slowly during early and midgestation and then rise more rapidly the third trimester and an especially sharp rise in estrogen levels occur the last few days of gestation, except in the queen. In the sow there is a temporary rise in estrogen levels around 12 to 30 days of gestation and in the mare from 150 to 250 days of gestation. In the mare this rise corresponds to the increase in size of the fetal gonads. In the mare and bitch estrogen levels in the dam's plasma declined slightly the latter stages of gestation.

Initiation of parturition in the ewe, doe, sow, cow, bitch and probably the queen starts in the hypothalamus of the fetal brain, possibly from stimuli such as placental aging, nutritional and uterine restrictions to growth and the accumulation of waste products, followed by release of ACTH from the pituitary gland and the elevation of adrenal cortisol in the fetal and then maternal plasma.^{21,33,49,97,98} The manner in which the different species respond to this elevated cortisol level differs. In ewes the placental enzymes cause the placental progesterone to be made into estrogen. Blood levels of progesterone fall rapidly and placental estrogen causes the synthesis of PGF_{2a} and uterine contractions occur. In cows, does and sows, cortisol stimulates placental estrogen production causing uterine release of PGF_{2a} and the rapid involution or luteolysis of the corpora lutea, with a rapid decline in progesterone levels and subsequent uterine contractions. Cortisol production by the fetus late in gestation is essential for rapid lung maturation and pulmonary surfactant production necessary for the survival of premature or mature fetuses.¹⁹ In the mare a somewhat similar pattern may exist but a pronounced rise in fetal plasma cortisol levels just prior to parturition has not been shown to occur.^{21,47,54,64,76,85} Further studies are needed. At the time of parturition in the mare the blood progestagen level is quite high, as in the woman, but drops rapidly within 24 hours after birth. In the bitch progesterone levels fall sharply just prior to parturition and cortisol levels reach a peak during the day prior to the onset of parturition. There was sharp fall of 0.8° C in body temperature of the bitch during the 24 hours prior to parturition.^{22,23} In the bitch and queen there is need for further studies to determine the exact sequence of events that initiate parturition. Prostaglandin E₂ as well as prostaglandin F_{2a} is found in the fetal fluids and plasma during the latter stages of gestation in the mare and other animals. The former prostaglandin probably plays an important role in maintaining the fetal vascular system including the patency of the ductus arteriosus^{60,85} and dilation of the cervix.^{63b}

It is likely that a synergistic action between the rise in estrogens and relaxin, the rapid decline in progestogens and the rise in prostaglandins (PGF_{2a}) precipitate peristaltic uterine contractions, cervical dilation and parturition. In sows a large amount of relaxin from the lutein cells of the ovaries is released the last few days of gestation. Prostaglandin stimulates release of relaxin that dilates the cervix, increases the pelvic area and facilitates the expulsion of the fetuses.³⁶ Relaxin levels in plasma rise rapidly late in gestation and just before parturition from 4.2 to 7 to 8 ng/ml. in the mare,^{94c} from 2.7 ng. to 42 to 257 ng/ml. in the sow^{90b} and in the cow.^{77b}

These levels decline very rapidly after parturition. During the second stage of labor in all domestic animals high levels of PGF_{2a} are present and as the fetus engages in the birth canal oxytocin is released. The latter hormone from the posterior pituitary gland does not initiate parturition as previously believed but augments it by stimulating the release of large amounts of PGF_{2a} .^{49,51,77a,98} However it is important, together with PGF_{2a} , in causing peristaltic uterine contractions to assist in delivery of the fetus(es) and the placentas. Two to 3 IU oxytocin i.v. intensified normal myometrial activity in sows within 20 seconds but 10 IU caused uterine spasms for 10 to 15 minutes.^{12b} Recent studies established that estrogens are important for myometrial sensitivity to oxytocin. This is accomplished by the regulation of the concentration of oxytocin receptors in the myometrium by estrogens.^{41b,93} Within 24 hours after birth, progesterone and estrogen levels in maternal plasma drop to very low levels in all domestic animals.

Postponement of parturition can be achieved by progestins in cows, ewes and sows for a few days to a week but dystocia and poor viability of the neonate often occurs. For short term postponement of parturition for a few to 18 hours, long-acting sympathomimetic, betamimetic or tocolytic agents such as clenbuterol or isoxsuprine may be used to produce myometrial quiescence.^{6b,c} These agents are not currently available to veterinarians in the U.S. (See Dystocia.)

Induction of Parturition (and Abortion)

The great increase in knowledge in recent years of the endocrine control of parturition has enabled veterinarians not only to produce abortions at nearly any stage of gestation in most domestic animals (See Chapter V) but to induce essentially normal parturitions by the timely injection of certain hormones. The stage of pregnancy at which parturition is induced, although not critical for the dam, is very critical for the welfare of the neonate.^{33,35} When parturition is induced prematurely more than 3 days in the sow, 5 days in the ewe and doe and 7 to 14 days in the cow satisfactory lactation and neonate survival and growth is severely affected. In the mare the mammary glands should be enlarged and developed and secreting a milk-like colostrum, the mare should be at least 330 or more days into gestation and the cervix and pelvic ligaments should be relaxed before parturition is induced.^{54,55,78,84} Because there are very few reasons for induction of parturition in the bitch and queen, few studies have been performed.

The principal reasons for inducing birth is to terminate the pregnancy and to allow delivery of the fetus(es) dur-

ing the daytime when trained skilled assistance is available. Other indications might include: a history of prior poorly viable neonates, prolonged gestation, abdominal hernias or severe edema, severe arthritis, possible injury or obstructions of the birth canal, fetal death or mummification and dropsy of the fetal sacs. There is no evidence to suggest that induced parturition can be more normal than natural birth. Therefore veterinarians should be both cautious and selective in their cases before recommending it and then carefully monitor the process. As animal owners are understandably prone to be highly critical should any adverse incidents occur to the dam or offspring during or for a long period after the induced birth (See Chart 2).

In mares the site for induced foaling should be in a clean, disinfected, quiet, isolated location. The most common technique or method is the injection of 20 to 100 IU of oxytocin into the mare with the criteria noted above.^{55,78} Forty to 60 I.U. given intramuscularly will usually result in a foaling within one hour. Recent studies have shown that much lower doses are probably safer even if a second or third dose at 30 minute intervals are needed to initiate the second stage of labor.^{77b} In mares ready to foal oxytocin in a dose as low as 0.5 to 10 IU caused the rapid release of endogenous PGF_{2a} and the initiation of labor within 90 minutes. Thus large doses greater than 10 IU may be unnecessary and even dangerous.^{77a} Large doses might cause uterine and muscle spasms,^{12b} premature placental separation or malposition of the fetus. The fetal membranes are usually noted at the vulva within 30 minutes. The fetus may be checked at this time or earlier to note and correct, if necessary, the position and posture of the fetus. The hormonal patterns produced by induction with oxytocin are similar to those occurring during a normal parturition.⁵⁴ Retained fetal membranes or subsequent infertility has not been experienced after inducing foaling in mares when the proper procedures were followed at full term.

As described in Chapter IV, the hormonal pattern at the termination of pregnancy in mares is very similar to that in women and different from the other domestic animals. A recent report on parturition in humans, causes one to speculate on a similar pattern in mares.^{41b} Namely, under the influence of estrogens during pregnancy there occurs a dramatic increase in myometrial oxytocin receptors. This lowers the threshold so rather small doses of oxytocin probably from the fetus activates myometrial activity and contractions as well as producing prostaglandin from the placenta where oxytocin receptors have also greatly increased. Prostaglandin release is essential for the dilation of the cervix and both hormones further promote uterine contractions and birth through the relaxed cervix.

Chart 2a. Hormones Used Effectively for the Induction of Parturition**

Species	Corticoids		Estrogens	PGF _{2α} and analogues	Oxytocin
	single administration	multiple			
Cow	+++*	+++ ¹ *	+	+++*	0
Ewe	+++*	n.n.	+++*	+++	0
Doe	++	n.n.	+++*	+++	0
Sow	±	+++	n.t.	+++*	0
Mare	±	+++	n.t.	+	+++*

¹May be necessary to assure the delivery of fetus; can be replaced by a single dose of a long-acting corticoid.

n.n. = not necessary; single injection fully effective.

n.t. = not tested.

*Presently most preferred technique.

Dose levels: Corticoids: Two to three times the optimal therapeutic dose.

Estrogens: Large therapeutic doses, repeated if not long-acting.

PGs: Equivalent or larger than the luteolytic dose in cycling animals.

Oxytocin: 20–100 I.U., repeated small doses, 5 to 10 I.U. preferable.

Legend: +++ = 90–100% effective; ++ = 70–90% effective; + = 60–80% effective; ± = ca 50% effective; 0 = not effective.

**Modified from W. Jöchle.⁶¹

Chart 2b. Condition of the Fetus and the Maternal Endometrium and Response to Hormonal Induction of Parturition (close to term, in delayed, or in pathological gestations) in the Cow.*

Condition of the conceptus ²	Condition of the maternal endometrium	Corticoids	Estrogens	Prostaglandin F _{2α} and analogues
Fetus alive, normal developed, approaching term.	normal	+++	+	+++
Fetus alive, normal developed, delivery delayed	normal	+++	+	+++
Fetus dead (shortly before term).	unknown	0	+++	+++
Dropsy of the fetal sacs: hydrallantois and/or hydramnios.	unknown	+++ ¹	+++	+++
Fetus died and is mummified.	normal	0	+++	+++

Legend: +++ = 90–100% effective; + = 60–80% effective; 0 = ineffective.

¹Depends on stage of gestation and viability of fetus.

²When fetal viability is unknown or fetus is dead, combined therapy of 2 or more hormones is probably indicated.

*Modified from W. Jöchle.⁶¹

Ordinary to large daily doses, 10 to 40 mg., of the glucocorticoid, dexamethasone, for 4 to 5 days did not induce foaling in mares late in the gestation period. However, when massive doses of 100 mg. of dexamethasone were given daily for 5 days from 321 to 324 days of gestation parturition occurred 3 to 7 days after the first injection.³⁴ Estrogens to induce foaling in mares has not been adequately investigated. Estrogen and dexamethasone given 24 hours before giving PGF_{2α} to mares between 325 and 354 days of gestation with none showing impending signs of foaling resulted in induced normal parturition 3 hours after the third dose of PGF_{2α} given

at 12 hour intervals.¹⁰² The prostaglandin analogue, fluprostenol, when given intramuscularly to mares (1000 ug) or to pony mares (250 ug) not showing imminent signs of foaling, produced the first stage of labor within 30 minutes and normal foaling occurred within 90 minutes in mares that were apparently hormonally ready for induction.⁸⁴ Further study on the use of prostaglandins to induce foaling in mares is indicated but presently oxytocin is the drug of choice.^{77a}

In sows induction of parturition may be produced by exogenous dexamethasone or PGF_{2α} or prostaglandin analogues.³⁵ Injection of dexamethasone results in a con-

siderable variation and a longer time period to produce delivery. While the prostaglandins, 10 to 12 mg PGF_{2a} , 175 ug **Cloprostenol** or 5 mg **Prostalone**, if given on days 111, 112 or 113 of gestation, preferably the latter two days, results in delivery of pigs in an average time of 33 hours.^{35,42,50,56} About 80 percent of the sows treated with PGF_{2a} farrowed within the predicted 12 hour period and 95 percent within 48 hours. When parturition was induced before day 111 of gestation in sows, unacceptable neonate losses resulted due to prematurity and poor viability.^{33,35} Thus if accurate breeding records with identified sows are available, treatment early one morning results in nearly all sows farrowing during daylight hours the next day when attendants are available. Farrowing could be planned for groups of sows 3 days a week, avoiding weekends and holidays. Cross-fostering of pigs would be more efficient. Induced farrowing might aid in reducing the incidence of M.M.A.^{16b,26} The prostaglandin analogues in sows, as in mares, produced less side effects of restlessness, rubbing and gnawing, salivation and increased respiration rates, defecation and urination than PGF_{2a} .²⁷ Following the administration of prostaglandins, progesterone levels decline rapidly due to luteolysis of the corpora lutea. During the day after the injection of prostaglandin about two hours after a stream of milk could be expressed from the teats or 28 hours after the injection of **Cloprostenol**, 50 IU of oxytocin will markedly shorten the time to birth.¹⁰⁵

In cows 16 to 30 mg of dexamethasone or 5 to 10 mg of flumethasone induced parturition after day 265 of gestation in over 80 percent of the cattle. The time from treatment to parturition ranged from 30 to 60 hours. Fifty to 90 percent of the cows had a retained placenta.^{33,60,104} Evidence would indicate that the glucocorticoid stimulated the release of estrogen from the placenta followed by the release of PGF_{2a} by the uterus which caused luteolysis. Treatment with estrogen, 25 mg of estradiol, before or at the same time as the injection of a glucocorticoid increased the percent of cows delivering, tended to shorten the time to delivery of the fetus and somewhat reduced the incidence of retained placentas.^{12,88} However the problem of estrogen residues in milk limits the use of this hormone in dairy cattle. The local treatment and manipulation of the retained placenta accompanying most cases of induced parturition in cattle should be avoided but parenteral injections(s) of antibiotics were indicated. The fetal membranes dropped from the uterus within 10 days and subsequent delayed conception and infertility was not a problem.^{33,60,104}

The injection of 20 to 40 mg of prostaglandin F_{2a} into cows after 265 days of gestation induced parturition in 90 to 100 percent within 57 to 100 hours. The time from treatment to delivery was longer with prostaglandin F_{2a}

than with the glucocorticoids.^{33,60,63} The incidence of dystocia was somewhat higher, the percent of live calves slightly lower and the incidence of retained placenta about the same as with the glucocorticoids. Estrogens will also induce parturition in dairy cattle but high doses of 100 to 150 mg of diethylstilbesterol or its equivalent must be used and residue problems would occur.⁶⁰ Combinations of a glucocorticoid, 25 mg dexamethasone, and PGF_{2a} or prostaglandin analogues, 500 ug **Cloprostenol**, have been used to produce abortions within 4 to 6 days in 93 to 100 percent of heifers from 1 to 8 months of gestation.^{6c} In New Zealand over 1 million late-calving dairy cows were induced to calve up to 3 to 5 weeks before term for economic and managerial reasons by the injection of a slowly absorbed corticosteroid formulation of betamethasone. Treated cows were observed carefully for parturition and periparturient disease problems. Retention of the placenta was commonly observed. It was determined there was no economic benefit to such a practice unless the cows were normal, young and healthy and advantages were indicated beyond the first lactation.^{71b} **Cloprostenol (Estrumate)** at a dose of 500 ug IM in cows and heifers from 250 to 300 days of gestation induced parturition in 95 percent of 64 animals within 0 to 60 hours, average 47 hours. It was desirable to induce parturition within one week of the expected calving date. Retained placenta occurred in 62 percent of the cows and 91 percent of the calves were viable.^{61b}

Thus both the glucocorticoids and prostaglandins reliably induce parturition in cattle after 265 days of gestation. Until further extensive comparative trials are conducted the glucocorticoids appear to be more desirable and safe in producing shorter gestation periods, none or very slight, increase in calving difficulty, slight reductions in birth weights, healthy viable calves and a reduced udder edema in dairy heifers and cows.⁸⁸ Heifers tended to have a shorter time interval from treatment to delivery than cows.⁶³

In ewes given 20 mg of estradiol benzoate at 142 to 148 days of gestation 65 percent lambd within 48 hours and 84 percent lambd within 96 hours.¹⁶ This treatment could not be recommended because of the high incidence of lamb mortality in the 16 percent of the ewes that did not respond to the treatment. In another trial ewes were given either 2 mg flumethasone or 15 mg prostaglandin F_{2a} on day 141 of gestation.⁵² Eighty nine percent of ewes treated with flumethasone and 33 percent treated with PGF_{2a} lambd within 72 hours after treatment. The average or mean hours from the flumethasone treatment to lambing was 50.9 hours for those ewes lambing within 72 hours. Another study in which 2 mg of flumethasone was given to ewes on days 138 through 144 of gestation, 67 to 89 percent of ewes injected on days 140 to 144 of

gestation lambled within 72 hours after treatment. Of those ewes injected on days 138 and 139 of gestation only 31 to 41 percent lambled within 72 hours.⁸¹ These studies further emphasized the need for more trials with prostaglandins and the importance of accurate breeding dates and records. Although further evaluation is needed, the use of 10 to 20 mg of dexamethasone in ewes 140 days pregnant induced parturition, and pregnancy toxemia losses were reduced.^{2,57}

In does the administration of 15 mg PGF_{2a} at 140 to 142 days of gestation resulted in induced parturition within 36 to 70 hours. Retention of the placenta for up to 24 hours with secondary metritis occurred in a number of does.¹³ Induction of parturition in goats has also been produced with estrogens and glucocorticoids but because of a lack of economic interest extensive studies in the doe have not been made.^{33,60} The doe responds to the above hormones in a manner similar to that of the cow to produce luteolysis and a rapid drop in progesterone levels with subsequent delivery. Live birth only occurs when estrogen and PGF_{2a} treatments are given after day 139 of gestation.³³

The Stages of Parturition

Although the act of parturition is continuous, for purposes of definition it is usually divided into three stages or phases.

First Stage—This stage is characterized by the relaxation of the cervix and active contractions of both the longitudinal and circular muscle fibers of the uterine wall. In ewes, does, and possibly the other domestic animals, the collagenous structural nature of the cervix probably requires a mechanism involving an enzymic degradation of collagen to cause cervical relaxation and softening. This is apparently brought about by a declining progesterone level, an elevated estrogen level and an elevation of prostaglandins. The latter are probably within the cervix.³⁶ In the sow and possibly the other species relaxin also plays an important role in cervical relaxation.^{21,33,49} The elevated levels of estrogen and prostaglandin and reduced progesterone induced in most species by an elevated level of glucocorticoids in the fetus result in uterine contractions. Oxytocin is seldom released from the hypophysis prior to the second stage of labor so is not essential for the induction of parturition or labor.^{21,38,49,69,101} Uterine peristalsis starting in the apices of the uterine horns is initiated by circular muscle contractions synchronized by propagation of the action impulse through the longitudinal muscles. Uterine contractions perform 90 percent of the work of parturition and

these contractions are directly proportional to fetal resistance. There is a greatly increased activity of the uterine musculature the last 1 to 2 hours before birth. The average prepartum amplitude of uterine muscle contraction was 80 cm. of H₂O. Uterine contractions force the fetal membranes and their fluids against and into the relaxed cervix. The external os of the bovine cervix relaxes sufficiently a week or so before calving to accommodate 2 to 4 fingers.⁴ The cervix of heifers remained tightly closed until the day before parturition. In the first stage of parturition the cervix was not dilated by the allantois chorion but was pulled open by the contraction of the longitudinal uterine muscles. For most of the first stage the cervix easily contained the allantois chorion that projected into it. True dilation of the internal os started 2 to 4 hours after the external os had reached a diameter of 8 to 12 cm and by 6 to 12 hours the whole cervix was 12 to 15 cm wide and the cervix and vagina were a continuous canal filled with the distended allantois-chorion. Once cervical dilation is complete, the bovine fetus is expelled within 2 to 4 hours unless fetal or maternal causes for dystocia are present.⁹²

During the first stage in the cow, uterine contractions occur about every 10 to 15 minutes and last 15 to 30 seconds. As the stage advances they increase in frequency, strength, and duration until contractions occur about every 3 to 5 minutes.^{8,46} In uniparous animals the contractions start at the apex of the cornua while the caudal part does not contract but rather dilates from the pressure of the fetus and fluids forced caudally. In this stage in the mare^{4,85} and probably the bitch the fetus is rotating from its dorso-pubic or dorso-lateral position into the dorso-sacral position. As it passes through the cervix into the birth canal the legs and head are extended. In the bovine and ovine fetus no rotation is necessary, as it is already in a dorso-sacral position. By the end of this stage the cervix is completely dilated.

The multiparous animals have a more complex mechanism of uterine contractions.^{4,8} The contractions of the uterus occur just cephalad to the most caudad fetus forcing it through the cervix into the birth canal, while the rest of the uterus remains quiescent. Then the same process is repeated for the most caudad fetus in the other horn, or the fetus immediately cranial to the one just expelled. This may help explain why in the second stage two fetuses may be born nearly simultaneously. The longitudinal fibers of the parts of the horn just emptied contract, but the circular fibers remain relaxed, so that the next fetus may pass through. This shortens the uterus as parturition progresses, so that each fetus in turn is brought back nearly to the cervix. This is important in multipara so that the fetuses at the apex of the uterine horn do not have to traverse a long uterine horn after the placenta

has been detached or the navel cord ruptured. The normal and abnormal behavioral patterns, or ethology, of the various species of animals before, during and after parturition has been described.^{39,40}

During this first stage of parturition which lasts about 1 to 4 hours, straining or labor is not exhibited in the mare. The symptoms of restlessness, anorexia, colicky pains, slight sweating behind the elbows and around the flanks, lying down and getting up, tail switching, elevating of the tail, repeated periodic sudden complete arrest in motion even chewing, repeated stretching as if to urinate, frequent small bowel evacuations, and looking at the flank are characteristic of abdominal discomfort in the mare during the latter part of this period. Usually the pulse and respiratory rates are accelerated. During the latter part of the first stage just prior to labor the mare may roll back and forth in an apparent effort to rotate the fetus into a dorso-sacral position. Both fetal and maternal activity and movements result in the turning or rotation of the fetus.⁸⁵ The mare may crouch, go down on her knees, rise again and be highly restless. The body temperature may become slightly lower than normal during this period.⁴

In the cow and ewe the symptoms of abdominal pain or discomfort may not be evident especially in pluriparous animals. In heifers, colicky symptoms and restlessness usually are observed and may last for 1 to 24 hours. The cow and ewe will show anorexia, stand with an arched back and raised tail, strain occasionally, and ruminate irregularly. The cow may lie down and get up frequently. Pulse and respiratory rates increase but lowering of the body temperature is inconstant.

In the bitch, sow, and cat nervousness, anorexia, and an increase in pulse and respiratory rates usually occur. In dogs this may result in panting. The signs of various stages of parturition in the bitch have been described.⁴¹ Occasionally vomiting is observed. This stage usually lasts for about 2 to 12 hours. In the dog there is usually a sudden drop of 1 to 2° F in body temperature to below 100° F just before or during this phase of parturition.

A drop in body temperature of 1 to 1.5° F just before parturition in cows, ewes, sows and bitches has been reported.^{22,23,30,31,32,107} This decline in temperature is related to the decline in progesterone levels. However because of its variability under field conditions, this fall in body temperature is of little practical value in predicting the onset of parturition in the cow, sow or ewe. In all animals in which a drop in body temperature occurs during this first stage, the temperature afterwards rises and reaches a peak during and shortly after parturition due to exertion.

This first stage is apparent for longer periods in pri-

miparous than pluriparous animals. During this stage in some animals of all species, milk or colostrum may drip or run from the udder. Usually toward the end of this first stage the allantois chorion ruptures as it is forced through the dilated cervix into the vagina. After the allantois chorion ruptures, the amnion pushes into and through the cervix, and the fetus—because of the shortening and contracting of the uterus and dilation of the cervix—passes into the cervix and vagina. Once a portion of the fetus enters the pelvis, reflex stimuli result in straining or labor. This is produced by contractions of the abdominal muscles and diaphragm together with a closing of the glottis; and the second stage of parturition begins.

Presentation, Position and Posture of the Fetus—

It is essential for the sake of accuracy to describe the various presentations, positions, and postures a fetus may assume at the time of its entrance into the birth canal or pelvis. These definitions were established by Williams¹⁰⁶ and are commonly used in the description of both normal and abnormal births.

The **presentation** includes: (1) The relation of the spinal axis of the fetus to that of the dam. Presentations are either longitudinal or transverse. (2) The portion of the fetus that is approaching or entering the pelvic cavity or birth canal. This portion of the fetus is anterior or posterior in the longitudinal presentation, or dorsal or ventral in the transverse presentation.

The **position** includes: (1) The relation of the dorsum of the fetus in longitudinal presentation, or the head in transverse presentation, to the quadrants of the maternal pelvis. These are the sacrum, the right ilium, the left ilium, and the pubis.

The **posture** signifies the relation of the extremities, or the head, neck, and limbs, to the body of the fetus. The extremities may be flexed or extended or retained beneath, on the right or left side, or above the fetus.

In outline form the presentation and position include all possible variations of the manner in which the fetus may enter the birth canal at parturition.

Presentations	Positions
Anterior, longitudinal	Dorso-sacral Right dorso-ilial
Posterior, longitudinal	Left dorso-ilial Dorso-pubic
Transverse ventral	Right cephalo-ilial
Transverse dorsal	Left cephalo-ilial

The normal presentation in uniparous animals is the anterior longitudinal presentation, dorso-sacral position with the head resting on the metacarpal bones and knees of the extended fore legs. Birth can take place without assistance if the fetus is in the posterior longitudinal presentation, dorso-sacral position. Unless the fetus is small, other positions result in dystocia. The transverse presentation is seen only rarely in ruminants and multipara. It can occur in the mare, in which the fetus develops in both horns, rather than in the body and one horn. Dystocia invariably results. The posterior longitudinal presentation, dorso sacral position, with the hind limbs retained or extended beneath the body, is commonly spoken of as **breech presentation**. Two old terms, only rarely used, are "sterno-abdominal" presentation, which is a transverse ventral presentation in the mare, and "poll" presentation which is an anterior longitudinal presentation, dorso-sacral position, with the head flexed beneath the neck. The position of the fetus in the uterus was discussed in Chapter 4. Thirty to 40 percent of the fetuses of multipara are presented posteriorly and this is considered normal or physiological. Because of the short neck of swine fetuses, the head and neck are seldom deviated. Since the limbs in multipara are small, short and flexible, their posture is of no importance. They may be extended beneath or in front of the body or flexed without resulting in dystocia. In ewes 69.5 percent of fetuses were in normal anterior presentation with the extremities extended and 17.8 percent of the fetuses were normal except for one retained or flexed leg.⁴ In sheep, fetuses may be expelled without assistance in anterior presentation with one fore limb extended beneath or alongside the body. When both forelimbs are retained beneath the body dystocia usually results.

The Second Stage—This stage is characterized by uterine contractions, the entrance of the fetus or fetuses into the dilated birth canal; rupture of the allantoic sac; abdominal contractions, or labor; and the expulsion of the fetus through the vulva. In the cow abdominal contractions occurred only after the feet of the fetus were in the cervix or vagina.⁴⁶ Breaking of the allantoic sac caused a sudden increase in abdominal contractions that were superimposed on the crest of each uterine wave with amplitudes of 80 to 320 cm. H₂O, average 180 cm. H₂O. In the cow and mare following the rupture of the allantoic sac, the amnion is pushed through the cervix and may appear at the vulva as a translucent distended membrane.⁸⁵ During this second stage of labor, uterine contractions occurred in the cow about 4 to 8 times every 10 minutes and lasted 80 to 100 seconds.^{8,46} Intermittent tenesmus or straining continues and the feet of the fetus appear at the vulva. As the feet pass through the vulva

the amniotic sac usually ruptures. Point pressure rather than diffuse pressure such as that exerted by the allantoic sac is the stimulus to abdominal contractions. Passage of the head, shoulders and hips of the fetus through the pelvis caused an increase in abdominal contractions. The fetal head starts through the vulva and at this point the greatest and strongest abdominal straining in the birth process usually occurs. In the larger uniparous animals as the head is being forced into the vulva, the chest is entering the pelvic canal. Often after the head passes the vulva the dam will rest for a few minutes before beginning straining again with strong abdominal efforts as the chest passes through the birth canal and vulva. The hips usually follow through the birth canal fairly rapidly but occasionally the hind limbs may remain in the vagina until the fetus or dam moves.⁸⁵ In goats and cows during the passage of the fetus through the birth canal and when the vagina was dilated there was a great increase in the levels of oxytocin in the jugular blood over that present during the first and early second stages of labor when in general it was similar to the very low blood levels present during pregnancy.^{38,101} The release of oxytocin during most of the second stage of labor was continual in contrast to spurts in the release of oxytocin during the milking act. Oxytocin causes the release of prostaglandins which further increases uterine contractions and cervical dilation.^{47,51,85} The levels of oxytocin in the blood plasma of goats, sheep and cows during the second stage of labor was 77 to 381, 5 to 3000, and 400 to 1000 microunits per ml., respectively. The half life of oxytocin in the blood is one to one and one-half minutes. In the goat the posterior pituitary gland contains about 9 to 13 units of oxytocin and about one-tenth that amount is released during parturition.^{38,101} Passage of the fetus through the birth canal not only causes the release of oxytocin but also the release of prostaglandins in the mare⁸⁵ and probably the other domestic animals.

Almost all animals lie down as soon as straining commences. The foal or calf may be born with the dam standing in only about 1.5 percent of mares and cows.^{85,92} The mare and sow usually lie out flat with the legs extended, whereas the cow, bitch, and ewe are more likely to lie on their sternum. In the mare straining is usually characterized by several, 2 to 5, strong expulsive efforts followed by 2 to 3 minutes of rest. This procedure is repeated at fairly regular intervals. In the mare one foreleg of the fetus precedes the other by 6 inches as the fetus passes through the birth canal.⁴ This indicates that one elbow and shoulder enters the birth canal before the other. The foal's cheek is usually lying on the limbs with its muzzle midway between the knee and fetlock joints. Although parturition is quite rapid in the mare it is ac-

companied by such great expulsive efforts that the mare is usually exhausted and will lie on her side for 15 to 30 minutes before rising.^{83,85} Since the umbilical cord in the mare is long it often does not rupture as the fetus passes through the birth canal. It will remain attached to the fetus for an average of 8 to occasionally 30 minutes until the mare or foal moves, when it breaks at a point about 3 to 5 cm from the foal's body. Pulsations can usually be felt in the umbilical artery for one to 9 minutes. If the umbilical cord is separated immediately 400 to 1,500 ml of blood is lost to the fetus.⁸³

In the cow the straining is not as forceful or as frequent as in the mare. During the early part of labor the cow may remain standing. Its body temperature may increase to a high normal level and the pulse and respiration rate will rise due to the exertion, as is observed in other animals. In the ewe the second stage of birth is similar to that in the cow. Once the second stage begins the abdominal contractions develop with gradually increasing frequency and intensity until birth has occurred. The periods or bouts of abdominal straining occur every 2 to 3 minutes and consist of 5 to 8 abdominal contractions in the cow. These abdominal contractions will increase and resting time decrease as the fetus enters and passes through the birth canal.⁹² If these contractions become reduced in number or intensity usually assistance will be necessary to deliver a live fetus, as this condition does not occur in normal deliveries. Once the feet have passed through the vulva they should stay there and not appear and disappear at each abdominal contraction. This same pattern is followed in other domestic animals.

In the bitch the amnion as it appears at the vulva before the first pup is usually broken by the bitch as she licks the vulva. In the bitch the delivery of the head through the vulva requires the greatest expulsive efforts. The umbilical cord, which is still intact at birth, is usually broken by the bitch. After the birth of each pup the bitch rests, licks the pup and her vulva. When the fetal membranes are expelled—in about 10 minutes after the birth of the pup—they are eaten by the bitch. It is probably best to let the bitch eat only 2 or 3 placentas and then remove the rest, as consumption of too many placentas may cause vomiting and diarrhea. The greenish-black fluid that is discharged following the fetal membranes is normal and is due to the breakdown of blood resulting in the presence of bile-like pigments, uteroverdin, around the edges of the placental zone of attachment. Straining begins again after 0.5 to 1 hour or more and another pup is expelled. Although it may take about 1 hour of labor for the first pup to be born, the periods of straining for the second and third pups are usually progressively shorter. The rate of expulsion of the fe-

tuses is very irregular. Some bitches may not expel the second fetus for several hours after the first. Then the next 2 or 3 may be expelled rapidly within 10 to 30 minutes of each other followed by another delay. Rarely are the pups expelled rapidly in a short time. They may also be expelled at somewhat regular intervals. The sow and queen have a second stage of birth similar to that in the bitch. The period of time between the expulsion of pigs varied from 3 to 45 minutes or rarely longer. The longest intervals were observed between the first and second pig and before the last pig.^{4,61,69} About three-quarters of the pigs were born with the umbilical cords intact and it took 2 to 6 minutes average time before rupture. After farrowing the sow usually urinates copiously.

In multipara the fetuses are expelled in an irregular and random manner from each horn, that is, one fetus may be expelled from one horn and then 2 or 3 from the other and then 2 from the first and one from the second, and so forth. In the bitch, but not the sow, the horn containing the most fetuses expelled the first fetus.⁹⁵ About half of the pigs born came from the same horn as its predecessor and the other half from the opposite horn.^{25b} In some sows most of one horn would empty and then all of the other and the remainder of the first horn and etc. In general porcine and canine fetuses came randomly. Porcine fetuses occasionally passed each other within the horn or uterine body and as many as 20 percent of the fetuses changed their presentations in late gestation or during parturition.⁹⁵ In 73 canine fetuses marked by transuterine injections at laparotomy between 45 and 54 days of gestation, 56.2% were in anterior and 43.8% were in posterior presentation. Between marking and birth 6.9% changed from posterior to anterior presentation. At no time did a canine fetus located more tubally pass another fetus located closer to the cervix. After the birth of one pup, the next pup came from the contralateral horn in 78.2% of the births. Therefore the two horns did not alternate in presenting a fetus into the birth canal. In the 14 bitches in their first to third parities the average duration of gestation was 62.3 days and the duration of parturition from the first to last pup ranged from 100 to 875 minutes (1.6 to 14.5 hours). Eight of the 14 bitches were given 1 IU oxytocin during parturition with 33.3%, 66.6%, 71.4% and 88.1%, of the pups born within 30, 60, 90 and 120 minutes, respectively of its predecessor.^{101b}

The presence of a dead fetus may delay the emptying of that horn. Occasionally in the mare, bitch, and only rarely in the other domestic animals, the fetus may be born with the amnion or a portion of it wrapped around its head. In the mare this may cause suffocation of the foal if not promptly removed. In carnivora, death is not

likely from this cause since the bitch and queen promptly licks and eats the amnion.

During this stage the contracting and shortening uterine walls force and direct the fetus into the birth canal and pelvis and abdominal contractions, or labor, drives the fetus through the birth canal. The intra-uterine pressure in the cow was 66 mm. of Hg between uterine contractions during the second stage of labor. The pressure reached about 170 mm. of Hg at the time of abdominal contraction. Thus the total pressure at the opening of the pelvic inlet is about 150 to 170 lbs., or about what one man could apply by traction on the fetus.⁷

The intra-abdominal pressure, caused by contraction of the abdominal muscles and diaphragm and closure of the glottis, is equal in all directions. The uterus is necessary to direct the fetus into the path of least resistance—the pelvic canal. If a large hernia is present abdominal contractions could force the uterus into the hernia. Not uncommonly traumatic gastritis or displacement of the abomasum may occur as a sequelae to parturition, due to the abdominal pressure. A healthy fetus, intact abdominal walls and a healthy uterus are necessary for normal birth.

In uniparous animals the large fetuses pass through an arc from the abdominal cavity upward into and through the pelvis and then downward again as they pass through the vulva. In the cow the fetus must pass over the high ischial tuberosities. This arc-like direction of the fetus as it passes through the pelvis causes stretching of its dorsal and pelvic muscles and a relaxation of the linea alba and abdominal muscles. The latter is important because it allows the pelvis to be extended backward on the fetal sacrum, thus reducing the sacro-pubic diameter of the fetal pelvis. The downward direction of the cranial portion of the fetus as it passes the vulva tends to push the fetal pelvis high in the maternal pelvis, where the bisiliac diameter is greater. This helps prevent a hiplock condition frequently encountered when traction is incorrectly applied. In hiplock the greater trochanters fail to pass between the shafts of the ilia.

The time for this second stage of birth in the cow is from 0.5 to 3 to 4 hours. In pluriparous cows this second stage usually requires 0.5 to 1 hour. Primipara may take longer, up to 3 hours or more. In ewes and goats the second stage of labor is completed in about 1 hour, range 0.5 to 2 hours, or slightly longer if twins or triplets are present. In mares this second stage is normally completed in 5 to 60 minutes with an average of 20 minutes.^{4,83,85} In multiparous or polytocous animals the length of the second stage of birth is variable, often depending upon the number of fetuses in the uterus. In the bitch the expulsion of the first pup may take up to 1 hour and

a variable time for each fetus thereafter. The average total time for the second stage of parturition in a bitch is 3 to 6 hours. Twelve hours would certainly be near maximum. In the sow the second stage is usually completed within 1 to 5 hours but occasionally may last up to 8 hours. In the sow the interval between the birth of pigs averaged 15 minutes but ranged from 1 minute to 3 hours.⁸⁶ A longer time interval between pigs often precedes the expulsion of a stillborn fetus. In the queen the time required to complete the second stage of labor is usually 1 to 2 hours with several minutes to an hour interval between kittens. In some cases delivery of fetuses may occur several days apart.²⁰ In the sow and bitch after the second stage of parturition is completed they actively nurse their young, cease straining, and are quiet and content.

When the umbilical cord ruptures, the two umbilical arteries together with the urachus retract into the abdominal cavity of the fetus. By the contraction of the arteries into the body tissues, provision is made for the prevention of bleeding from the navel. The umbilical vein collapses, the blood drains from it and the fluids in the umbilical cord drain out, often aided by the licking of the cord by the dam. The umbilical cord becomes necrotic, dries up and drops away in 7 to 21 days.

The Third Stage—The third and last stage of parturition is the expulsion of the fetal membranes and the involution of the uterus. These two conditions are discussed separately because the expulsion of the fetal membranes is normally completed within a few hours after the expulsion of the fetus, whereas involution of the uterus to its normal nonpregnant state may take more than a month in some species.

Fetal maturity is synchronized with parturition by the decline in progesterone and the elevation of prostaglandin and cortisol in the doe and ewe and the other animals. This alteration in hormone levels late in gestation also results in placental "maturation" and the initial early changes which after fetal birth result in the rapid separation of the fetal and maternal tissues at the microvillous junction and the initiation of lactation.^{24,94,98}

Expulsion of the Fetal Membranes—With the birth of the fetus, the vessels in the fetal placenta collapse and the villi become small and shrunken. After the expulsion of the fetus the uterus still contracts strongly for 48 hours and less vigorously, but more frequently, thereafter.^{46,62,92} This is necessary to prevent hemorrhage and to aid in the expulsion of the fetal membranes. These peristaltic and contraction waves besides reducing the size of the uterus and aiding in forcing the placenta and membranes into the birth canal probably markedly reduce the amount of blood circulating in the endometrium. This

causes a dilation or relaxation of the maternal crypts. The shrinking of the villi and the dilation of the maternal caruncular crypts probably play a major role in the separation of the fetal trophoblast and cryptal epithelium of the maternal placenta. No maternal tissue is shed in the afterbirth of cows. However a few fetal villi may be caught and left in the maternal crypts.¹⁰ The middle uterine artery immediately contracts following parturition. The artery becomes thickwalled and the characteristic thrill of "whirring" is absent although it may be several weeks or more before it involutes to near its normal size. In exceptional cases an aneurism of this artery may occur and a thrill or "whirr" may be palpated over a portion of the artery for several weeks or longer following parturition. The uterine contractions during this third stage produce movement of the uterine wall and caruncles that may aid in freeing or separating the fetal placenta. There is no muscular tissue in the caruncles. The weight of the amnion and the portion of the allantois chorion in the birth canal tends to help remove the afterbirth from the uterus. The incidence of retained afterbirth was much higher in buffalo in which the young were not allowed to suckle, 22.7 percent, than when the young were allowed to suckle, 4.9 percent.¹⁰³ It is well-known that suckling stimulates the release of oxytocin from the pituitary gland. A lack of progesterone during the last month or so of pregnancy resulted in the occurrence of parturitions 10 to 20 days earlier than normal together with a high incidence of retention of the placenta.^{69a,69b} Early parturition, twin pregnancy or a shortened gestation period have frequently been observed associated with retained placenta. In these instances infection may play a pathogenic role. This will be discussed further under retention of the fetal membranes. Normal expulsion of the fetal membranes can be said to be a complex process involving both mechanical and hormonal factors, although the exact mechanism is still not completely understood.

In bitches and queens the fetal membranes are usually expelled irregularly between the fetuses; or one fetus may be expelled with its own placenta and that of a fetus expelled earlier. In rare instances expulsion of a few placentae may be delayed for 12 hours or more. In the sow, since a number of the allantois chorions may be fused, the fetal membranes may be expelled at only 2 to 3 intervals during parturition. Most porcine afterbirths were expelled from 20 minutes to 12 hours, average 4 hours, after the birth of the last pig.⁶¹ Occasionally placentas were retained with no observed ill effects. The fetal membranes of the last fetuses in the bitch are usually expelled shortly after the birth of the last pup. This third period of labor is characterized by relatively short, infrequent, and mild periods of straining usually at the time

the larger mass of membranes are expelled or when much of the placenta is hanging from the vulva especially in uniparous animals. In most unipara the amnion and umbilical cord start through the birth canal first and as the allantois chorion separates from the endometrium at the apex of the horn due to peristaltic waves starting there, the chorion or fetal placenta is inverted and the allantoic surface is outside as the membranes are expelled from the uterus.⁶² If placental expulsion is delayed for a longer period of time than normal the chorion of fetal placenta may be exposed when it falls from the vulva. Occasionally when fetal expulsion is delayed the fetal placenta may separate, and later both the dead fetus and the fetal membranes are expelled or withdrawn together. Unlike the mare, placental separation in the cow is slower than in most other species of animals, so that the second stage of labor can be prolonged without the danger to the fetus. The umbilical cord of the bovine fetus is ruptured as the fetus passes through the birth canal. In the cow the length of time required for the expulsion of the fetal membranes is normally 1/2 to 8 hours. The ewe is similar to the cow. The mare normally expels its fetal membranes within 0.5 to 3 hours after the birth of the foal. Generally, the healthier the animal the more prompt is the expulsion of the fetal membranes. Domestic animals, with the exception of the mare, will usually eat the expelled fetal membranes. Instances of cow's choking and suffocating while eating their placentas have been reported.^{100a,106} Ruminants will not eat their fetal membranes if the membranes are decomposed. Multipara usually eat the fetal membranes as well as any fetal cadavers. The act of eating the fetal membranes is not known to be beneficial in any way. In ruminants the placenta may lie in the rumen and slowly macerate or decompose over a period of several weeks or more and is occasionally suspected of causing indigestion. This is questionable, since nearly all cattle eat their fetal membranes and symptoms of indigestion or toxemia rarely occur. Occasionally the cow may begin eating her fetal membranes before they have dropped away from the uterus. After the expulsion of the fetal membranes in a normal birth, the cervix secretes a rather thick tenacious mucus that tends to seal the cervix and thus helps prevent infection gaining entrance to the uterus.

Involution or regression of the uterus in domestic animals, with the exception of the cow and the ewe, has not been extensively studied. In multiparous animals and the ewe, rebreeding the female within the next 1 to 6 months is seldom practiced. In the bitch, sow, and queen estrus usually does not occur until after the young are weaned. In the sow signs of estrus may be exhibited about 3 days postpartum but if copulation is allowed the conception rate is extremely low. In the mare, commonly

bred 9 to 30 days after foaling, relatively few studies have been made on the involution of the uterus. Regression of the mare's uterus proceeds at a rapid rate.^{3,94b} The endometrium, however, had seldom completely involuted by the onset of the foal heat. In many mares the endometrium must be largely restored by the third to fifth day after foal heat or 12 to 17 days postpartum when the early embryo enters the uterus. Conception often occurs from service at this estrum. By 13 to 25 days after parturition the endometrium was fully restored in all normal foaling mares. At the time of onset of foal heat the subepithelial areas of glandular epithelium were highly disorganized and contained large number of leukocytes. This would indicate the uterus was not yet in a completely involuted and normal state. However, after placental separation the uterine epithelium is relatively undamaged and by 7 to 10 days after a normal foaling involution of the endometrium is largely completed.^{94b} By the end of foal heat both the gross and microscopic involution was nearly complete.^{48b} The mare may discharge a slight amount of grey to brownish lochia for about one week postpartum. Involution appears more rapid in primiparous mares than in pluriparous mares. Exercise appears to hasten involution. The rapid involution of the endometrium in the mare and sow is probably related to the simple diffuse placental attachments. The genital tract of all mares became infected, usually with streptococci, at the time of foaling or within one to three days. In normal mares this infection was overcome soon after the onset of foal heat or about the sixth to tenth day after parturition.¹⁴ Pregnant sows from 30 to 100 days of gestation may be aborted within 34 to 42 hours by a single dose of 500 ug. cloprostenol, a prostaglandin analogue. Estrus occurred in these sows within 9 to 10 days and breeding on this first heat resulted in 90% conception.^{78a} Therefore uterine and endometrial involution in the sow is rapid as in the mare.

In cows the involution of the uterus has been carefully studied.^{7,15,17,66-68,73,74,79,92} Following the expulsion of the fetal membranes in the cow the uterine contractions and peristalsis continue as strong rhythmical waves that gradually diminish through the fourth day. In the cow the uterine muscle cells shortened from 750 microns after parturition to 400 microns one day later. From the fourth to eighth days there are only irregular undulations of the horn.⁷

The maternal placenta involuted by the necrosis of the caruncular stalk due to vasoconstriction, leucocytic infiltration and by the dissolution of the uterine caruncle by fatty infiltration, solution, sloughing and detachment of the entire superficial layer of the caruncle that became part of the uterine lochia.^{43,68,79} The caruncle and its stalk were necrotic by the fifth day after parturition. The dis-

solution and sloughing of the caruncle was generally completed by the twelfth day leaving a raw surface with protruding blood vessels where the stalk was attached. The caruncles had returned to nearly their original size by the second or third week. This delayed loss of maternal placental tissue through necrosis would lead to the observation that cattle and sheep are not true nondeciduate animals. By about 25 to 30 days postpartum, epithelium covered the caruncles and repair was complete. Thus a 70 gm. caruncle by 48 hours after birth reduced its size and weight to 26 gms. and was quite small 5 days later. Even when the caruncles are nearly normal in size at 30 days postpartum a large vascular bed of vessels remains. These feel rather fibrous and are present for a long period even if the animal does not become pregnant. The intercaruncular epithelium may be eroded by bacterial lysis but is normally repaired by 20 days postpartum.^{65,67}

The lochia in the bovine uterus the first 48 hours after parturition was greatest in amount of any period, about 1400 to 1600 ml. By the eighth day postpartum the amount had decreased to 500 ml. and by 14 to 18 days there were only a few ml. of lochia. The amount of lochia discharged from the vulva was variable. Most primipara discharged about 50 ml. Some primipara discharged almost no lochia but absorbed it from the uterus. Some pluripara discharged from 800 to 2000 ml. of lochia. Usually this discharge of uterine lochia, consisting of mucus, tissue, detritus, and blood, commenced about 3 to 4 days postpartum and increased until the ninth day. The detritus was light yellow-brown to red in color. After the ninth to tenth day postpartum, there was an increased amount of blood mixed with the lochia. This apparently originated from the surface of the caruncles. This bloody lochia usually ceased about the twelfth day. Hyperleukocytosis was found only the first 2 to 3 days postpartum. The process of normal involution took the course of an aseptic process. However, in the examination of apparently normal cows. A spontaneous puerperal infection causing a massive bacterial growth in the uterine lochia was often observed.⁷⁹ About 93 percent of bovine uteri were infected from parturition to 15 days postpartum, 78 percent between 16 and 30 days, 50 percent between 31 and 45 days and 9 percent between 45 and 60 days.²⁹ Lymphocytes were extremely numerous in the endometrium of infected uteri and only moderate in most bacteriologically sterile uteri.⁴⁴ In puerperal cows infections due to *C. pyogenes*, *E. coli*, staphylococcus, *Pseudomonas aeruginosa*, streptococci, or mixed infections were most commonly cultured. These infections in cows resulted in the lochia assuming a white, yellow-white or grey mucopurulent character toward the latter part of the puerperal period. Vaginal exudates of 5 to

200 ml. volumes in 30 to 35 percent of all cows were reported 10 to 20 days postpartum but only 2 to 5 percent had this volume at 30 to 50 days.⁹⁶ These latter cases were probably those with persisting infections.

Plasma levels of prostaglandin metabolite were high for 7 to 23 days postpartum. Cows with postpartum uterine discharges had longer periods of prostaglandin release, 16.7 days, and longer periods for the completion of uterine involution, 39.6 days, than the cows with a normal postpartum uterine involution 13.5 and 29.6 days, respectively. Progesterone levels remained at baseline levels in the postpartum period until the prostaglandin release had ceased.^{64a} The interval from parturition to complete involution of the uterus averaged 29.6 days (range 16 to 50 days). Prostaglandin increased uterine tone and promoted involution.^{64a} Presence of ovarian cysts had little or/no effect on uterine involution.

The involution of the bovine uterus and cervix based on rectal palpation during the postpartum period was reviewed and reported upon.^{73,74} The size of the bovine uterus decreased slowly between the fourth and ninth days postpartum. By the tenth day the involuting uterus could be completely defined by rectal examination. A marked decrease in uterine size and an increase in uterine tone occurred from days 10 to 14 coinciding with the onset of the first estrus in normal cows and the voluminous discharge of the uterine lochia. Fluid or lochia could be detected in the uterus by palpation on days 7 to 12 postpartum in many cows. During this period of 10 to 14 days postpartum the size of the postgravid uterine horn declined from 12 cm to 7 cm in diameter. The rate of uterine regression was quite rapid from 14 to 25 days postpartum. There was a decreased rate of involution between days 26 and 39. Between days 40 and 50 there was little change noted. Prior to day 20 postpartum the diameter of the cervix, 4 to 7 or more cm, was smaller than the horn and after days 22 to 25 the cervical diameter, 3 to 4 cm, was greater than the horn diameter.^{73,74,96} The following postpartum regression in the weight of cows' uteri was 10 Kg. at parturition, 5 Kg. at 6 days, 2 Kg. at 12 days, 1 Kg. at 25 days and 0.7 Kg. at 50 days.^{65,68} Within 24 to 36 hours after a normal parturition the hand could not be passed through the cervix and by the fourth day postpartum only two fingers could be introduced. If a retained placenta was present the rate of closure of the cervix was delayed and the hand could still be inserted at 48 hours and often at 72 hours postpartum. In general the major gross palpable or physical involution of the uterus occurred by 25 to 30 days postpartum. Changes after 30 days were much less marked and more gradual. A summary of reports on bovine uterine involution as determined by palpation showed the time for involution varied from 26 to 56 days post-

partum with a majority of authors reporting complete regression between 42 and 47 days.^{73,74,92} Clinical and rectal examination of the genital tract and ovaries of normal post partum dairy cows revealed the first estrus to occur about 15 days after calving with the second estrus occurring about 33 days postpartum after a somewhat shortened estrous cycle. Subsequent estrous cycles were a normal length. Great variations were observed in high-producing cows and those with abnormal parturitions. Silent estrus occurred in 77 percent of the first postpartum ovulations, 54 percent of the second and 36 percent of the third ovulations.⁷⁴ Hormonal profiles of individual dairy cows during the postpartum period of 40 to 78 days varied greatly but correlated fairly closely with clinical findings. The first preovulatory LH peak occurred at an average of 17 days (± 10 days) and the first estrus occurred on postpartum day 28 (± 16 days).^{88a}

During the spring and summer months cows' uteri involuted more rapidly than cows calving during the fall or winter months. Cows suffering from periparturient diseases such as retention of the afterbirth had a slightly slower rate of uterine involution. The normally regressing uterus did not become histologically normal until 50 to 60 days postpartum or about 20 days after the uterus had returned to a clinically normal or involuted state. Following a retained placenta leucocytic infiltrations occurred in large numbers and remained for 20 to 30 days beyond the normal histologic involution in normal parturition or until about 70 to 90 days postpartum. Corpora albicantia replacing the corpora lutea of pregnancy usually are larger, containing more connective tissue, than are corpora albicantia replacing corpora lutea that were active for only a short period of time. In some cows these may persist for a number of years. In nearly 20 percent of the cattle, resorption of the corpora albicantia occurred after the fourth pregnancy.^{25a}

Postpartum involution of the canine uterus is a prolonged process extending over a 12 week (3 month) period. Although the interplacental area returns to normal within a few weeks, the placental sites require many weeks to involute and heal.^{2b} But as late as 3 months after parturition, when the uterus is the size and appearance of the normal diestrous uterus, slight pigmented ring-shaped stripes may be observed in the endometrium indicating the former placentation sites. The bitch discharges much dark, mucoid, green lochia after parturition. This green pigment is uteroverdin and comes from the "green border" of the placenta.³⁷ This color is produced by the breakdown of hemoglobin. This decomposition product is the same as bilirubin and biliverdin. In the cat the placental border is brown. The first week the lochia is amber to red in color and by the second week it should be normal, clear mucus. The walls of the gravid horn

remain slightly thickened. In primipara and other young animals the uterus never returns to its pregravid size.

The rate of involution in the other animals is not as well known but in sows a lochial discharge may be observed for about a week and involution of the uterus was fairly rapid.⁷ The uterine mucosa of the ewe was completely involuted by 30 days after parturition and the process was described in detail.^{100b} The uterine weight of postpartum ovine uteri was 700 gms at 3 days, 200 to 250 gms at 7 days, 60 gms at 21 days, and 30 gms at 35 days.⁷⁰

Artificial Interference in Normal Parturition

If parturition is a normal one there is no need or necessity for outside aid by attendants. Such aid is ill-advised. In the artificial environment under which many domestic animals are kept certain sanitary and preventive precautions may be necessary. Valuable animals should be observed during the act of parturition so that injury to the newborn is not caused by the dam or the surroundings, such as a mare or cow trying to give birth with its rear quarters wedged into a corner of a box stall. The afterbirth of ruminants should be removed after its expulsion so that the dam will not eat it or choke on it. Following parturition it is highly essential that the dam and newborn not be disturbed for several hours so that close "bonding" between them can occur.^{56b} If the dam becomes excited after parturition, or for some other reason attacks the newborn, they should be separated. This condition is seen occasionally in the sow, the "berserk" sow, and in rare cases in the dog, in which the dam kills and even eats her young. The young cow may rarely attack her newborn offspring. Upon arising and feeling the placenta against her hocks or heels the mare may become excited, kick, and possibly injure the foal. Some horse men tie up the amnion to the umbilical cord so the membranes are not stepped on and torn.^{83,85} Occasionally in young mares, heifers, gilts, and ewes the udder may be so sensitive, edematous, and sore that they will not allow the newborn to nurse. After dystocia or for other unknown causes, females may reject, ignore, or fail to accept and nourish their young. In these cases the dam must be restrained or given a sedative or tranquilizer to allow the newborn to suckle or colostrum must be given and the newborn placed on a foster mother or fed milk replacer. If the cow or mare gave birth in a box stall, the wet, contaminated straw should be removed and replaced with clean, dry straw. If parturition took place in an unsanitary environment the navel requires disinfection.

It is desirable to have a comfortable, quiet, isolated,

sanitary place in which the animal can give birth. The dam and the newborn should be left alone unless the course of parturition is definitely abnormal. Close observation and knowledge of the normal course of parturition is necessary. If the first stage of parturition in the cow, doe and ewe is over 6 to 12 hours, in the mare over 4 hours, in the bitch, queen and sow over 6 to 12 hours; or if the second stage of parturition in the cow, doe and ewe is over 2 to 3 hours, in the mare over 20 to 40 minutes, in the sow, bitch and queen is over 2 to 4 hours, outside help is indicated. If at anytime the normal progression of the fetus(es) into and through the birth canal fails, assistance is usually needed. This should be obtained at once if severe injury to the dam or death of the fetuses is to be prevented. This aid to the dam is indicated if the frequency or intensity of abdominal contractions declines before the birth of the young or if the feet of the fetus in unipara appear and disappear with each labor contraction without progress in the passage of the fetus. In posterior presentation in primiparous, uniparous dams, outside traction may be desirable to avoid asphyxiation of the newborn. The help or assistance provided at parturition should be competent and experienced.

During the act of parturition it is not desirable or necessary to rupture the fetal membranes, either the amnion or allantois. It is not desirable to apply traction in physiological birth when the fetus first appears at the vulva. Such traction is likely to result in laceration and trauma of the dorsal commissure of the vulva or the perineum. Traction if applied too early before the cervix, vagina, or vulva is fully dilated, pulls these structures caudally and makes the lumen or diameter of the birth canal smaller, requiring trauma or rupture of the structures if birth is to be accomplished with traction. Williams stated, "In an experience exceeding 60 years I do not recall vulvar or perineal laceration in physiological birth in a domestic animal when not tampered with by attendants." There is no indication for or advantage to the administration of oxytocin before or after normal parturition. The umbilical cord should be allowed to break of its own accord in the mare. In the cat and bitch the dam usually bites it off or it breaks off naturally by traction. Ligation of the umbilical cord in animals is usually unnecessary and frequently predisposes to umbilical infection.

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Parturition and Involution

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Care of the Newborn and the Dam

At the time of the birth of the young especially in the mare, an attendant should be present to remove the amnion that may be wrapped around the muzzle and nose and cause asphyxiation. The onset of fetal respiration

may begin before the fetus is completely expelled in some parturitions, especially those that are delayed. In normal parturitions respiratory movements in the fetus are initiated by several deep inspirations about 10 to 60 seconds after expulsion. In the foal this will often occur before the umbilical cord has ruptured. It is believed that either a rise in the CO₂ levels in the fetal blood,⁷ an increased hydrostatic pressure in the fetal vessels when the cord ruptures, or removal of the amnion from over the nostrils, or a combination of these factors initiates breathing in the newborn. If respiration in the newborn is delayed various procedures should be used to stimulate this activity. The mucus should be removed from the nose and mouth. The newborn should be laid on its side on straw, not loose chaff or shavings that might be inhaled, with the head and fore quarters slightly lower than the hind quarters. Vigorous rubbing of the newborn with straw, hay, towels or shaking its head, or tickling its nostrils, will help bring about respiratory activity. The use of an oxygen tank and an attached short rubber tube has proven useful in saving some weak newborn. The tube is passed into the pharynx and the nostrils and mouth are closed tightly. Oxygen under moderate pressure distends the lungs. Opening the nostrils and pressure on the chest collapses the lungs and the process is repeated as often as necessary. A positive pressure "Bird" respirator may also be used. A warm oxygen tent or chamber may help save some weak pups or kittens. In recent years several simple resuscitators with attachments for an oxygen tank are commercially available. These actively remove excess mucus from the lungs and provide oxygen. Other practices, such as artificial respiration, have not proved very satisfactory or saved many weak newborn animals. Electrocardiographic studies showed a rapid rise in the heart rate occurred at birth, from 54 to 60 to 108 to 216 beats per minute in the equine newborn and from 72 to 108 to 96 to 120 per minute in the newborn calf.¹¹⁰ Some veterinarians advocate dipping the pup or kitten in cold then hot water to stimulate respiration. Other workers advise holding the young up by their hind legs to aid cleaning mucus from the larger bronchi, throat, and nose. If this is done in the newborn calf a copious flow of mucus is often passed from the nose and mouth. Most of this mucus obviously must come from the stomach. It has been observed by the author that in the handling of nearly all newborn which at expulsion are so weak that respirations do not begin normally within 1 to 2 minutes, any treatment of a drastic nature is often unsuccessful, although such efforts are usually indicated and are appreciated by the owner.

Umbilical disinfection may not be necessary if births occur on clean pasture. The licking of the navel and the

absence of barn or barnyard infections usually ensure the rapid and normal healing of the newborn's umbilicus. If parturitions take place in a barn or barnyard, particularly if navel infections are prevalent on the farm, careful disinfection of the navel may help prevent disease. It is doubtful if a hasty, careless application of a disinfectant or antiseptic to the navel will be of any value. To be effective an antiseptic should be carefully applied 1 to 3 times daily for the first two days following birth. Tincture of iodine, 1:1000 solution of alcoholic sublimate, 5 percent tannic and 5 percent salicylic acid in 70 percent alcohol, 10,000 ppm. neutral iodophor solution, 40,000 to 50,000 ppm. sodium hypochlorite solution with a very low hydroxide content, or any similar antiseptic, may be applied by carefully soaking the navel stump and squeezing it with cotton soaked in the antiseptic. Some prefer to use a powdered astringent such as alum or tannic acid and an antiseptic. This is carefully dusted on the navel stump to hasten dessication. In foals it is often advisable to administer a prophylactic dose of tetanus antitoxin. Two foals developed tetanus even though the dam received a booster injection of tetanus toxoid during pregnancy.⁸³ A contributing factor may have been that both mares leaked milk for a week before parturition. In a valuable newborn, antibiotics such as penicillin, streptomycin, tetracycline, ampicillin or chloromycetin may be administered for several days to prevent navel infection or septicemia. Clean, sanitary, well-bedded stalls for the calf and parturient cow help greatly in preventing navel infections. On farms or ranches where large numbers of females give birth in a confined area sanitation practices and facilities are highly important to prevent navel infections, infectious diseases of the newborn as well as retained placenta, metritis and mastitis in the dam. If young calves are placed together they may suck the umbilical stumps and cause navel infection. In countries with the screwworm, *Cochliomyia americana*, infestation during the warm seasons, it may be necessary to treat the navels of newborn animals with a fly repellant to prevent screwworm infestation of the navel stump.

The newborn should nurse and thus get colostrum within 1 or 2 hours after birth. From birth to suckling averaged 111 minutes, range 35 to 420, in the foal⁹³ and an average of 10 to 35 minutes, range 3 to 153, in the pig.⁶⁰ In the sow this may be slightly delayed if the pigs are removed as they are born—to prevent their injury by the sow—and returned after parturition is completed. The great importance of globulins in the colostrum, which are only absorbed from the gut 12 to 36 hours after birth by the newborn animal, has been discussed under placental transfer of immunity. This does not occur in domestic animals except to a slight degree in the dog and

cat.⁵⁰ Under highly unsanitary or infected environmental conditions, it is desirable to get colostrum into the newborn promptly, within 15 to 30 minutes after birth. If necessary this may be given by stomach tube. The amount of colostral antibodies absorbed and available to the newborn is in direct proportion to their levels in the colostrum and the amount of colostrum consumed within a few hours after parturition. Premilking in cows, sometimes practiced to avoid severe edema of the udder, may reduce the immunoglobulins available to the newborn calf because of their dilution in large quantities of milk stimulated by this practice. The principal transfer of globulins from the blood to the milk occurs the last 3 days of the gestation period.⁹³ Besides the important immune bodies absorbed from the colostrum by the intestines during the first 24 to 36 hours of life there are laxative properties in the colostrum. In the cow the colostrum is about five times as high in protein, two times as high in fat and minerals, ten times as high in iron as ordinary milk. In the newborn lamb this first feeding of colostrum is essential to getting it on its feet, and making it strong and active. Clipping of the udder in heavily fleeced ewes may aid the lambs to find the teats and nurse promptly. If for some reason, such as preparturient leaking of milk, colostrum from the dam is not available, another source may be indicated. Colostrum may be frozen and stored for such emergencies. In calves and foals 1500 to 2000 ml. should be given in divided doses the first 12 hours after birth.^{22b} The amount of immunoglobulins absorbed from the colostrum is directly related to the susceptibility of the newborn to the neonatal diseases of scours, septicemia and pneumonia. In 300 baby calves purchased at auctions, deaths occurred in 16 percent of calves with 1 to 6 percent of the serum protein comprised of gamma globulins while only 1 percent deaths occurred in calves with 19 to 46 percent gamma globulins in their total serum protein fraction.⁵³ Eighty to 90 percent of neonatal foals with failure of colostral immunoglobulin transfer developed infections and died or required therapy. This was largely due, as in cattle, to low colostral immunoglobulin content.⁷⁷ If colostrum is not available a transfusion of plasma or of dam's blood or blood from an animal of the same species is indicated to provide the necessary antibodies.^{33b} Dam's blood should not be used in newborn where hemolytic diseases are suspected. In large animals 500 to 800 ml. of blood or serum is usually administered subcutaneously,^{22b} as large amounts of fluids are difficult to inject intravenously and the process frequently causes violent struggling in the newborn. In the smaller animals 20 to 100 ml. of blood or serum may be given. Lyophilized immunoglobulins may be prepared and stored and given by stomach tube to the newborn animal.^{33b}

The use of the antibiotics have been of further help in bringing these animals lacking immune bodies through the first few critical weeks of postnatal life. The newborn of animals except dairy cows and goats suckle the dam until weaned. In the sow each pig selects its own teat, the stronger often getting the better mammary gland, so that in a week or two there are only as many functioning glands as there are pigs. This teat preference occurs in kittens but not in pups.^{45,46} The other glands, that are not being suckled, involute. In uniparous animals the young suck all teats. There are many methods of managing the newborn calf to prevent digestive upsets or diarrhea, after he has suckled the dam for the first 12 to 24 hours.

The Problem of Handling and Feeding of Orphan Animals is occasionally presented to the veterinarian when the dam dies at parturition or fails to give sufficient milk. It is well known that the young of a species thrives best on milk of its own kind. Therefore having the orphan adopted by another postparturient female of the same species is indicated. This is fairly easy and can often be done in all domestic animals when such an animal is available. Occasionally it is necessary in the sow to make the young smell like the foster dam's offspring by rubbing her fetal membranes or genital discharges over the orphan, or sprinkling the entire litter of orphans and sow with a material having a similar strong odor such as a weak cresol solution or an aerosol deodorant. In sheep it is a common practice to cover the orphan with the hide of the dead offspring or the wool of the ewe that is to be its foster mother. In the large animals, as in cows, the foster mother usually adopts the orphan fairly promptly but occasionally she may have to be restrained for a number of times to permit feeding. In the dog most postparturient bitches will readily adopt the newborn of another. The problem is more difficult when a foster mother is not available. All domestic animals can be raised with proper care and attention by artificial nursing and feeding.

In calves the problem is simple, since cow's milk is nearly universally available. In the other animals the problem can be solved to a great extent by referring to Table 8 on the composition of the milk from the various animals. From this table it is noted that milk of the ewe, doe, and cow are nearly similar in composition. The milk of the sow is richer in fat. Mare's milk is similar in composition to human milk and foals therefore thrive on formulas for human babies. After foals are several months of age, cow's milk might be satisfactory; but younger foals may develop a stubborn diarrhea when fed cow's milk.⁸⁸ Pigs, pups and possibly kittens may be raised on rich cow's milk, evaporated milk, or prepared formulas.^{6b} Presently there are fortified powdered milk prod-

ucts for foals, "Foal-lac,"* for pups, "Esbilac,"* for kittens, KMR, and for pigs, "SPF-lac."* These are mixed with the proper amounts of warm water and fed as are the synthetic or formulated starters for calves. The milk should be warm and fresh. The newborn animal should be fed every 1 to 3 hours for the first week or so and then every 4 or 12 hours thereafter. The amount of milk fed daily to the young of cattle, horses, sheep, goats, and swine should be about 10 percent of the body weight, divided into the aforementioned number of feedings. In dogs and cats the feeding of orphan young is discussed in Chapter 9 following cesarean section in the bitch. All animals can be fed by nipple bottle with either calf, lamb, human, or doll nipples. At an early age most animals except lambs usually may be taught to drink milk from a shallow pan or bucket. If symptoms of diarrhea develop, the amount of milk should be reduced markedly for 24 to 48 hours and oral and parenteral antibiotic, electrolyte and supportive therapy should be instituted. In some cases one may increase the amount of milk gradually to more than 10 percent of the body weight after the first week or so of age. It is hard to starve a young animal, but easy to overfeed it. Orphan pigs may be reared on special commercial pig starters or formulas containing antibiotics.

The orphan young should be encouraged to eat solid food as early as possible so that the amount and frequency of milk feeding can be reduced. In general for the first 1 to 2 months of life the orphan young will not appear as well nourished as animals that are not orphans, and will more often have digestive disturbances. Care and nursing are of utmost importance in the proper rearing of orphan young on artificial diets; otherwise artificial feeding is not particularly difficult. In some cases the addition of vitamins, especially A and D, may be necessary or advisable. In pigs, iron may be provided by injections of an iron dextran product intramuscularly, painting the sow's udder with a weak solution of iron, or supplying clean soil to prevent anemia.

A Persistent, Patent or Pervious Urachus is invariably seen with infection of the navel either as a cause or a result of an open urachus. This condition is seen most commonly in the newborn foal and rarely in cattle. Since it is often followed by pyemia, septicemia, and navel or joint ill, the condition should be viewed seriously. Antibiotics administered over a period of 10 to 14 days is indicated together with local treatment of the navel with antibiotics or disinfectants. If, after several days, the urine continues to flow through the urachus keeping the navel and the surrounding skin moist, the lower 4 to 5 inches

of the urachus should be cauterized with a small swab containing Lugol's solution or the instillation of about 2 to 5 ml. of 5 to 10 percent formalin solution. This or similar treatments will usually swell and close the urachus.

Retained Meconium—In the newborn foal the meconium in the rectum may be found in hard pellets from 1/2 to 2-1/2 inches in diameter that within 24 or 36 hours after birth become impacted just cranial to the bony pelvis. The condition is seen more often in colts than in fillies. The diameter of the bony pelvis is very small in the newborn foal. The affected foal usually nurses normally but within 24 to 48 hours after birth exhibits symptoms of colic and persistent to intermittent straining, frequently getting up and lying down, elevating the tail and assuming a straddled attitude similar to that assumed during defecation. Colicky symptoms may become more severe, and anorexia occur. Impaction may be confirmed by inserting a lubricated finger into the rectum and palpating the mass of hard pellets of meconium. This disease is not uncommon in foals, and for that reason many veterinarians recommend that all newborn foals be given an enema soon after birth. This enema may be of physiological saline, mineral oil, olive oil, castor oil, mild soap and water, or several ounces of glycerin in a pint of soapy water; the author has found the commercial obstetrical lubricants like "Lubrivet" very satisfactory and nonirritating. About 4 to 6 ounces are introduced at a time through a soft rubber horse catheter. This may be repeated as often as necessary. In cases of impaction of meconium with colicky symptoms this may have to be repeated frequently at intervals of 10 to 30 minutes until the condition is relieved. Oral administration of laxatives such as castor oil, or the injection of "Lentin," is not usually indicated as the fecal material in the rectum and small colon behind the hard meconial pellets is soft. Gentle, persistent treatment usually results in recovery. Heroic or drastic treatment with a looped wire or forceps is dangerous and rarely necessary.

Rupture of the Bladder or Urachus may occur in rare instances in the newborn foal. This probably occurs due to a full bladder especially in male foals at parturition or when the navel cord is ruptured. The foal appears normal for 12 to 24 hours; but by the second to fourth day the foal is depressed, pulse and respirations are increased, and the abdomen is slightly to markedly distended.^{39,76,115} Tapping the abdominal cavity with a needle in a sterile manner will release the urine and confirm the diagnosis. Blood tests show a rise in blood urea nitrogen. Laparotomy on the midline, and repair of the ruptured bladder is indicated. Supportive and antibiotic therapy with good nursing often results in a successful termination.

*Borden Chemical Co., Box 419, Norfolk, Va. 23501 and other suppliers.

Many Congenital or Hereditary Conditions such as atresia ani, cleft palate, edema, undershot jaw, contracted tendons, blindness, cerebellar hypoplasia, and combined immunodeficiency (CID) and others may affect newborn animals. (See Chapter III). Some of these defects such as umbilical and scrotal hernias and cryptorchidism noted at birth may spontaneously recover within a few weeks to months. The observation and study of anomalies in the newborn is interesting. It may be of value to the owner, if the condition has occurred several times in a herd, to check carefully for inbreeding and for a hereditary recessive factor causing the condition. If the veterinarian is acquainted with the reported hereditary defects or anomalies in the newborn he may be able to advise his client properly even though only one defective individual has been produced. If the defects or anomalies are recognized early, treatment is possible in some; but in others slaughter must be recommended. Many anomalies or defects are observable at birth or cause noticeable symptoms to develop within several days after birth. Others may not be diagnosed for months or years.

Infections of the Newborn Contracted in Utero are rather uncommon compared to the infections contracted after parturition due to contact with virulent organisms in the outside environment. Many diseases of the newborn such as various septicemias, enteritis, pneumonia, and others may develop shortly after birth. A few of these diseases may be contracted **in utero** or in the birth canal at parturition. Probably most of them are contracted after birth from infected surroundings either through the raw umbilical or navel area, by ingestion or by inhalation. Many diseases of the newborn are favored by improper nutrition, management and housing facilities. The numerous infectious, managerial and nutritional problems affecting the newborn will not be discussed in this text inasmuch as they are not directly associated with parturition or gestation.

Most of the organisms known to cause placental and fetal disease with abortion may cause disease or infection of the newborn. Many of the organisms mentioned under causes for abortion may be present in fetuses born at term and cause their early or delayed death.

In cattle these include *Brucella abortus*, *Leptospira* spp., *Listeria monocytogenes*, *E. coli*, *Streptococci*, *Toxoplasma gondii*, *Aspergillus* spp., and *Salmonella* spp. Antibody titers for brucella, leptospira and IBR-IPV, influenza, BVD-MD and other viruses in the serum of newborn calves that have never suckled have been reported. This indicates a prenatal exposure and response by the fetus to these organisms whether the organisms can or cannot be recovered from the fetus after birth. There is evidence^{67,71,110} that *Mycobacterium*

paratuberculosis may be transferred **in utero** from an infected cow to its fetus and be carried into the postnatal period. Bovine leukemia virus, similar to feline leukemia virus may occasionally pass to the fetus **in utero** although most spread occurs horizontally.^{43,112}

In horses the fetal infections contracted **in utero** causing abortion, as well as early neonatal deaths after premature abortion, as well as early neonatal deaths after premature or term births, include: *Streptococcus zooepidemicus*, *E. coli*, *Actinobacillus* or *Shigella equi*,³³ *Leptospira* spp, *Salmonella abortus equi*, and rhinopneumonitis or herpesvirus 1.¹⁷ It may be difficult to determine in some infections, such as the first two, whether the fetus was infected before birth, during birth or whether the foal became infected soon after birth. If the newborn animals are visibly ill at the time birth or within a few hours then the infection was probably prenatal especially if retained placenta or metritis develops in the mare. Only 7 of 3,346 aborted fetuses yielded *Actinobacillus equuli* on culture but if postnatal death occurred within 24 hours of birth the *Actinobacillus* infection probably occurred prenatally.^{5,91,92} Intrauterine infection of fetuses with equine infectious anemia virus has been occasionally reported.

In swine prenatal infections that may cause neonatal infections or death include: *Leptospira* spp., *E. coli*, hog cholera virus,^{19,42} parvovirus, pseudorabies virus, *Toxoplasma gondii*⁹⁵ and *Eperythrozoon suis* (?).¹¹ Newborn pigs may become chronic carriers of the last five organisms. Poxvirus was recovered from pustular skin lesions in a newborn pig.⁸¹

In sheep and goats intrauterine infections that may be present in newborn lambs and kids include: *Vibrio fetus* var *intestinalis*, *Brucella melitensis*, *Salmonella* spp., *E. coli*, enzootic abortion or *Chlamydia*, *Toxoplasma gondii* and *Mycobacterium johnei*.¹⁰⁸ The latter organism is not a cause for abortion in sheep. Occasional intrauterine transmission of ovine progressive pneumonia virus and caprine leukoencephalomyelitis virus has been reported.^{22,28}

In dogs and cats neonatal infections that may be contracted **in utero** include: *Streptococci* spp., *Staphylococci* spp., *E. coli*, *Pseudomonas aeruginosa*, *Leptospira canicola*,^{64-66,70} canine herpes virus infection or "fading pup syndrome,"^{20,23} distemper virus, infectious canine hepatitis virus,⁷⁰ *Haemobartonella canis*,⁷⁰ and *Toxoplasma gondii*. The latter protozoal infection of prenatal fetuses has been reviewed in dogs and cats as well as in swine, sheep and cattle.^{95,102} In cats panleukopenia virus and leukemia virus may occasionally be transmitted **in utero**. The horizontal spread of these viruses in young and older cats is much more common.^{82,85}

Parasites Transmitted in utero from the Dam to the Fetus include:

In horses—*Strongylus vulgaris* larvae.¹³ This is very rare.⁹¹ A verminous aneurysm in a 2 day-old fetus was infected with *Actinobacillus equuli*. *Babesia caballi*.¹¹¹

Strongyloides westeri larvae may be transmitted to the foal in the dam's milk as early as 5 days after parturition. Anthelmintic treatment of mares with **Cambendazole** within a few days after foaling prevented infection of the foals for several weeks and reduced the incidence of "foal scours."⁷³ As noted below strongyloides in swine and hookworm and ascarid larvae in dogs may also be transmitted to the newborn in the colostrum.

In cattle—*Neoascaris vitulorum*,⁸⁷ *Theileria annulata*,¹¹¹ *Anaplasma marginali* (?),¹¹¹ *Cysticercus bovis*,⁷⁹ *Trypanosoma theileri*,⁹⁷ and *Fasciola hepatica*.⁸⁶ Many other bovine parasites may be transmitted to the fetus in utero.⁵⁶

In swine—*Strongyloides ransomi* and *Stephanurus dentatus* or swine kidney worm.^{8,104} Although a few reports indicated that *Ascaris suis* infection of fetuses may occur, several studies⁸⁴ proved that this does not occur.

In dogs—*Toxocara canis*,^{38,68,70} *Ancylostoma caninum*,^{1,70} and *Dirofilaria immitis*.^{70,75} *Demodex canis* infection of pups probably occurs the first few hours of life as there was no evidence it was acquired in utero.⁴⁸ Several therapeutic regimens used to obtain ascarid-free pups have been described.^{21,49} There is presently no treatment to prevent *Toxocara* larvae from migrating from the dam to the fetus during pregnancy.

Thus many bacterial, viral, fungal, parasitic and other diseases may be transmitted in utero resulting in the birth of infected neonates. In fact even rabies virus may pass transplacentally to fetuses of infected skunks.⁵⁵

Neonatal Isoerythrolysis, or Hemolytic Icterus of the Newborn, has been described in the horse, pig, dog and cattle. In 1948 this condition was described in foals.^{12,15,16,34-37} Many workers have done much to clarify the causative factors and describe methods of diagnosis and treatment.²⁴ An incidence of 1 percent affected mares was reported in the New Market area in England. Neonatal isoerythrolysis of foals occurs when mares become isoimmunized to certain types of erythrocytes either through (1) placental breakdown and absorption of the antigens from placental tissue or fetal blood at previous gestation periods or (2) by transfusions of blood or (3) injection of fetal tissue vaccines. When these mares are bred to stallions which transmit to the fetus the type of erythrocyte to which the mare was previously immunized the disease develops. The icteric condition occurs when the apparently normal foal suckles and receives in

the dam's colostrum large amounts of antibodies composed of hemagglutinins and hemolysins. Hemolytic icterus has very rarely been observed in foals from primiparous mares. It is usually not observed in foals until the mare's third or fourth parturition. Although most mares apparently become sensitized from the placenta of their foals. An early equine-fetal-tissue vaccine used for vaccination against virus abortion caused certain mares to be immunized to the erythrocytes in the vaccine.³⁶ Since vaccines prepared from equine tissues are not now used the incidence of neonatal isoerythrolysis has declined. Neonatal isoerythrolysis in foals is not due to an Rh-like factor as in humans but is caused by an isoimmunization of pregnancy due to intraspecies blood group factors (red cell antigens).

Recent studies^{4b,105b} on equine neonatal isoerythrolysis have shown that blood factors A and Q account for nearly all cases, especially in Thoroughbred and Arabian horses.^{105b} Brood mares possessing both blood factors A and Q are at low risk in producing affected foals. While mares lacking one or both factors and with a titer of anti-A or anti-Q of about 1:8 or 1:16 within 14 to 28 days of foaling are at high risk of having their foal develop this disease. Prognostic tests for these blood factors and their corresponding antibodies are now commercially available.^{4b,105b}

The symptoms, which may resemble foal septicemia, usually develop rapidly after the foal begins nursing, with mild to severe clinical symptoms occurring from 12 to 96 hours after birth. These include: somnolence; anorexia due to weakness; usually no rise in body temperature; increased pulse and respiration rate; slight to marked jaundice and anemia; and in severe cases prostration and hemoglobinuria. Foals which die rapidly have little icterus but an acute anemia. Foals that die of this disease after several days of illness usually show icterus and have severe liver and kidney damage.²⁴ Icterus is also seen in foals that do not show illness until several days after birth. Hemoglobinuria and hemoglobinemia are unusual symptoms. The red blood cell count drops from a normal of 10 to 12 million, down to as low as 2 to 3 million in the most severe cases. In severe cases the death of the foal may result in 24 hours or less. In slight or mild cases where the amount of antibody from the ingested colostrum is minimal, recovery may occur without treatment. The condition should be carefully differentiated from septicemia of the newborn usually characterized by elevation of temperature, injection and congestion of the conjunctiva with icterus being absent or slight. Cases of septicemia, if treated fairly early, usually respond to treatment with parenteral antibiotics while cases of neonatal icterus do not respond to antibiotic therapy. The

red blood cell count does not fall below 5 to 6 million in septicemia of the newborn.

The laboratory diagnosis was described by Bruner.¹² The technique of testing the blood of mares and their foals, and stallions to which the mare was to be bred is relatively simple with proper equipment such as a centrifuge and microscope. In agglutination tests, using the serum of mares and a 50 percent suspension of carefully washed red cells of the foal or his sire, if the serum titer of the mare is no higher than 1:2 and the colostrum titer no higher than 1:4, the foal may safely nurse its dam. If the serum titer of the mare is 1:4 or the colostrum titer 1:8 the foal is likely to develop icterus and may or may not recover without treatment. If the serum titer in the mare is higher than 1:4 or the colostrum titer is 1:16 or higher it would be dangerous for the foal to nurse its dam. The development of an hemolysin titer of 1:10 or more is apparently necessary to produce marked symptoms of the disease. The serum of sensitized mares may be tested against the red blood cells of a stallion and if a titer of 1:2 or less occurs the mare may safely be mated with that stallion. The prognosis in hemolytic icterus depends upon how early the condition is diagnosed and the promptness with which treatment is instituted. Advanced severe cases often die.

The treatment of clinical cases consists of promptly removing the foal from the mare or muzzling it. If symptoms are mild and the condition was not noted until the third to fifth day following foaling, treatment is unnecessary. In severe cases several blood donors should be obtained and the blood of the dam and foal tested against various donors' blood. If they are compatible, a large blood transfusion of 1500 to 2000 ml. of blood or more should be given the affected foal by injecting the blood into one jugular vein and removing an equal amount from the other by means of a 14-gauge needle. Occasionally another 500 to 1500 ml. of blood may be given the next day. In less severe cases 500 ml of blood may be transfused once or twice daily to carry the foal through the critical period of the disease which usually lasts only one to three days.²⁴ Transfusions are usually necessary when the symptoms of the disease are exhibited within 24 hours of birth; when the foal is weak and unable to stand; and when the red blood cell number drops below 4,000,000 per cmm. or 8 gm. of hemoglobin per 100 ml. of blood. Up to 7000 ml. of blood may be transfused in a large exchange transfusion in severe or critical cases. In practice this is often not possible and usually only about 50 percent of the foal's original blood is removed. The blood volume of horses and foals is 8.11 to 9.7 percent of the body weight or in the average foal about 4000 to 6000 ml. The administration of antibiotics and confinement to

prevent excessive exercise is advisable. The foal's dam should never be used as a blood donor. Because of the low incidence of blood factor A in Shetland ponies they should be considered as potential blood donors.^{105b}

The dam should be milked out frequently by hand or by allowing another older foal to nurse her.^{15,37,94} The newborn foal can absorb antibodies from its digestive tract for only about 36 hours after birth. It had been shown in earlier work that the first colostrum had the highest titer and that this titer dropped rapidly in 12 to 18 hours with frequent milking even though slight amounts were secreted for several weeks postpartum. Most authors reported that after 48 hours postpartum it is safe to allow the foal to nurse if the mare has been milked out frequently.

This disease in foals can usually be prevented if the sensitized mare is recognized because of having previously produced an icteric foal, or by testing the mare's serum against the red cells of the stallion to which it is to be bred. A positive test indicates that the disease will probably occur. A negative test is not significant as the mare may have become sensitized during pregnancy to the stallion's red cells. A better procedure is to test the mare's serum against the stallion's red cells the last month, or preferably the last week, of pregnancy.²⁴ Even if the stallion's blood is compatible with the mare's serum when tested before breeding, the foals of sensitized or isoimmunized mares should not be allowed to nurse until its red blood cells are tested with the mare's colostrum or serum. This is the most practical test. This may be done by immediately muzzling the newborn foal until the test is completed. If the foal's erythrocytes agglutinate in a 1:4 dilution or higher with the dam's serum or 1:8 or higher with the dam's colostrum, the foal should be fed either "Foal-lac," a human baby milk formula, low-fat cow's milk to which some sugar syrup and possibly lime water have been added at a rate of 1 ounce syrup and 1 ounce lime per pint. The foal may be placed on another mare for several days. On the larger farms banks of frozen colostrum permit the foal to be provided needed colostrum after first crossmatching the red blood cells of the foal and the milk. These foals should be given prophylactic treatment with antibiotics for 4 to 6 days. The dam should be milked out thoroughly at frequent intervals by hand or by an older foal. After 48 hours the dam's foal may be unmuzzled and allowed to suckle. Some veterinarians prefer to give the foal 500 cc. of compatible donor's serum to replace the antibodies lost to the foal by not nursing its dam the first 48 hours after birth. In the convalescent period injections of iron dextran intramuscularly may aid recovery. Once a mare produces a foal affected with neonatal isoerythrolysis, sub-

sequent foals are apt to be affected especially if the mare is bred to the same stallion. Recent further reviews on hemolytic icterus in foals have been published.^{37,58,90,94}

A similar condition has been described in dogs previously immunized by blood transfusions.^{44,107,116,117} Natural isoimmunization of the bitch during pregnancy is apparently rare. Although there are 7 blood types, A through G in the dog, only A is of significance in regard to incompatibility. In blood transfusions especially in breeding females, only A-negative donors should be used to avoid producing hemolytic disease in the pups after nursing. Leakage of blood from affected pups during parturition and subsequent uterine absorption may be one way of sensitizing the bitch.⁴⁴ The signs of hemolytic anemia in affected pups are similar to those in foals. Most severely affected pups die within 72 hours of birth. Not all pups in a litter are usually affected, only those with type A positive blood. Treatment involves withdrawing 10 to 15 ml of blood from the jugular vein of affected pups and replacing it with a similar amount of A negative blood. In affected bitches the pups should be fed formula and not be allowed to nurse the bitch for 36 hours after birth. After this period their gut will not absorb the antibodies present in the colostrum and they may be returned to their dam for nursing.^{66,99}

Neonatal isoerythrolysis also occurs in pigs from 1 to 7 days after farrowing.¹⁴ Similar signs to that in foals and pups of weakness, depression, paleness of mucous membranes, anemia, icterus, prostration and occasionally hemoglobinuria are noted in some pigs, but not all, in a litter. As in dogs this condition may only rarely occur naturally. Most porcine cases have been due to vaccination of sows with crystal violet or swine tissue vaccines against hog cholera. In a few cases mildly affected pigs recover without treatment. Probably several blood group antibodies can cause the condition in swine.⁴ Other excellent reports on this disease in swine have been published.^{18,79}

Bovine neonatal isoerythrolysis has been reported in Australia and the United States associated with the use of a vaccine that contains red blood cells as a preventive for tick-fever and an anaplasmosis ("Anaplaz") respectively.^{98,105} The proper use of the latter vaccine, that is, vaccinating only nonpregnant cows, reduces the incidence to a very low level while still providing a degree of immunity to the disease. Hemolytic disease of the newborn has not been described in sheep, goats and cats but is a possibility.

Nutritional deficiencies causing disease in the newborn animals include: (1) copper deficiency causing enzootic ataxia, swayback of demyelinating encephalop-

athy in lambs in Colorado, Peru, Australia, New Zealand and Great Britain. This is characterized by a progressive locomotor incoordination and partial or complete paralysis. Feeding additional, minute amounts of copper sulphate to the pregnant ewes prevents this condition.⁵⁹

(2) Iodine deficiency or excess causing enlargement of the thyroid glands or goiter is most frequently observed in foals. This may be prevented by feeding iodized salt and by avoiding the excessive feeding of iodides especially in the form of seaweed.⁶

(3) Selenium deficiency causes congenital white muscle disease or myopathy in newborn lambs in New Zealand and other countries.⁵¹ This condition has also been described in dogs,⁷⁴ and calves.⁶⁹ Myocardial degeneration and degeneration of skeletal muscles, especially of the neck, jaw and tongue are causes for weakness, inability to nurse and early death.

(4) Vitamin A deficiency causes increased susceptibility for infectious diseases. This may occur rarely in newborn animals whose dams have been on a vitamin A deficient diet for many months. The teratogenic effects of vitamin A deficiency on fetal development have been described previously.

Neoplasms of newborn animals are rare and have been reviewed.⁸⁰ Tumors of the skin included papillomas of equine fetuses, and subcutaneous melanomas; a subcutaneous mixed tumor and subcutaneous mixed tumor and a subcutaneous lymphangioma in bovine fetuses. Abdominal tumors included mesotheliomas of the peritoneum, a sublumbar lipoma and a retroperitoneal chondrosarcoma in bovine fetuses. As in adult animals, mesotheliomas of the abdominal cavity produced ascites and resulted in dystocia that was relieved by caesarian section. Neoplasms of the gonads included adenomas of the testicles and granulosa cell tumors of the ovary of bovine fetuses.⁶¹ Congenital lymphoid leucosis often with skin involvement has been reported most often in bovine fetuses and newborn calves, and occasionally in a newborn piglet and a feline fetus.¹⁰⁹ Other tumors included reticulosarcomatosis, carcinomatosis originating in the liver, nephroblastomas, a fibrosarcoma,²⁵ and teratomas. Congenital leucosis has been reported in fetuses in cattle and cats. Most cases of leukemia are caused by the horizontal spread of the virus between animals.

Miscellaneous diseases or causes of death of newborn animals include:

Persistent bleeding from the navel stump. This occurred more often when the cord was cut with a sharp instrument instead of being broken by traction. If ligation of the cord is necessary to prevent excessive bleeding then the newborn should be placed on parenteral an-

tibiotics for 3 to 7 days and the ligature removed in 24 to 48 hours. Repeated disinfection is indicated. A hemorrhagic disease of calves was reported⁴⁷ in which the dams were normal but had been fed sweet clover hay during the gestation period. Four newborn male and female calves from one dam bled severely from the navel after birth. Three of the calves died but one survived after repeated transfusions. These calves suffered from a multiple coagulation defect of their blood. A possible hereditary nonsex-linked character might have been present.¹⁰ Hemophilia in foals and pups have been previously described as affecting the male newborn in these species.

Fibroelastosis of the heart valves due to an unknown cause has been described in pups and kittens and rarely in calves causing enlarged hearts and deaths of the newborn within 2 to 3 months after birth.⁴¹

Respiratory distress syndrome and convulsions in Thoroughbred newborn foals have been described.^{93,94} These foals have been called "barkers," "dummies," "convulsives" and "wanderers" depending upon the signs exhibited. Several different etiological factors or diseases were present in these foals including asphyxia, trauma (cerebral hemorrhage) and fetal stress. The respiratory distress syndrome was described^{93,94} indicating the affected foals were normal for 24 hours. Respiratory distress began on the second day and became more severe. The respiratory rate went from 25 to 85 per minute. Inability to stand developed and extensor spasms occurred by the third day with death of the foals by the end of the third day or early on the fourth day. The lungs were atelectic and edematous with an absence of the surface-active lung lining or hyaline membrane. Thus this disease in foals resembled the respiratory distress syndrome in human infants and piglets. A lethal autosomal recessive condition in swine characterized by respiratory distress ("barkers") and hypothermia soon after birth together with hypothyroidism, hairlessness, myxedema, reduced adrenocortical activity and immaturity of lung tissue with a surfactant deficiency has been reported.^{115b} This syndrome resembles the condition in foals and humans but a genetic component has not been reported in these latter species.

Management and environmental conditions may cause or predispose the newborn to death or disease. Based on extensive and careful records 6 percent of calves die at parturition or within 25 hours of birth, 3 percent in multipara and 14 percent in primipara.¹¹³ There was a higher mortality rate in male calves and more abnormal parturitions associated with male calves. Calf mortality was eight times higher in moderately to severe abnormal parturitions or dystocia than in normal parturitions. The incidence of abnormal parturitions was twice as high for

male calves than for female calves. Certain sires produced calves having a higher mortality rate at parturition in primipara, 18 to 19 percent, than other sires, 8 to 10 percent.¹¹³ These sires should not be used on heifers. Dennis has reviewed the incidence and causes of perinatal mortality in cattle, sheep and horses.^{30,31} Martens^{75b} and Rosedale and Ricketts⁹⁴ have further reviewed the diseases and therapy of newborn foals. In a survey of 790 feline litters 10 percent of the fetuses were stillborn and 27.1 percent of the live kittens failed to survive to one year of age. Malformations occurred in 6.8 percent of the kittens.^{97b} In a study of inbred matings, calves from certain sires had a much higher postnatal mortality rate than calves from other inbred sires.²⁶ A higher than normal mortality rate occurred within several days after birth in Brahman cows calving on range during cold wet weather.³² A greater number of male beef calves were lost at parturition; these losses were greatest in primiparous cattle, 9.5%, and least in pluriparous cows, 2.4%.³

Pups, pigs and lambs, in fact all newborn animals, have a poikilothermic nature and are often unable to respond to cold by increasing their metabolic rate until 3 to 7 days of age. This is most noticeable in thin, underweight, malnourished, "runty" newborn animals where nutritional reserves are not present. Many of these neonates appear immature. As high as 30 percent of baby pig losses after birth were due to chilling.²⁷ It was also an important cause of death in pups.^{45,46} Hypoxia was the principal cause of 75 to 85 percent of stillbirths in swine.^{47b} High death losses in newborn lambs occurred when the weather was cold and especially when the lambs were small and undernourished.² Lambs weighing 4 pounds or less at birth suffered 65 percent or greater death losses compared to 5 to 8 percent losses in lambs weighing 10 to 14 pounds.^{54,100} High environmental temperatures during gestation and underfeeding caused the birth of smaller lambs. The mortality in twin lambs with lower birth weights is 30 to 40 percent higher than in single births. Other causes for mortality in the newborn is lack of vigor due to inbreeding, prematurity, lack of nutrition for the dam during the gestation period and a failure of the dam to own or accept her newborn.¹⁰³ Rarely certain Hereford cows may have such large teats that a small weak calf is unable to obtain colostrum. Occasionally postpartum dams suffer from agalactia due to disease, such as mastitis or endocrine causes and the newborn must be raised as an orphan. Disease factors causing mortality in lambs was carefully reviewed.⁹ Subcutaneous edema associated with low serum protein levels was commonly present in all pigs for the first two days after birth. This edema disappeared after the ingestion of colostrum raised the serum protein levels of the pigs.⁴⁰ Supplying artificial heat to the newborn and seeing that

colostrum is ingested early to supply both energy and antibodies will save many weak neonatal animals.

Injuries to the fetus during normal parturition are rare, but in dystocia forced extraction may result in **fractures of the fore or hind limbs**, especially in cattle. Fractures most often occur in the metacarpal or metatarsal bone in the region of the "break joint" or epiphysis, due to applying the chain or rope above the fetlock and placing a severe strain on the leg by twisting, jerking, or excessive traction. If the fetus is dead this is of no consequence but if the fetus is alive the fracture may be highly embarrassing for the veterinarian. By bandaging the leg and padding it well after correction of the displaced ends of the bone, and applying a plaster cast, the calf or young animal can walk. In 5 to 6 weeks this may be removed, and complete healing usually results. If a compound fracture occurs the prognosis is more guarded and antibiotics locally and parenterally are indicated.

Fracture of the jaw may result from excessive traction or twisting. Occasionally the snare or chain may slip forward and fracture the bony plate holding the incisor teeth, thereby causing them to point forward. In cattle these fractures are difficult to hold in place after correction. Frequently slaughter may be advised if both halves of the mandible are broken through the body, although surgery and wiring or pinning may be successful in selected cases. If only the incisor teeth are involved in the fracture, the animal will usually nurse satisfactorily or will drink from a pail, and healing occurs promptly even though the teeth may be at a more acute angle than normal.

Fractures of the ribs occur in foals due to injury of the fetus in its expulsion through the birth canal or due to the dam accidentally stepping on the foal. Dyspnea often develops within a day or two with a jerky painful respiration and an audible grunt on expiration. The foals move slowly and stiffly. Death often results. Occasionally taping the chest snugly with wide adhesive tape may be helpful if the lungs are not damaged.

Dennis²⁹ reported 174 hepatic ruptures and 1 splenic rupture in 4,417 lambs necropsied. Similar ruptures might occur in other species but they are rarely reported.

Dislocation of the hip joint is very rare in the newborn of the larger domestic animals. If excessive traction or twisting is applied to the rear legs in posterior presentation dislocation is possible in the pup. In anterior presentation of the fetus when the head protrudes through the vulva and the fetal body is wedged in the birth canal, twisting or excessive traction on the head may cause dislocation of the occipital joint and the death of the canine or feline fetus.

Subconjunctival hemorrhage is occasionally observed in newborn calves due to trauma during birth. If

the cornea is not injured, therapy is not necessary and recovery occurs in about 7 to 10 days.¹¹⁴

Edema of the tongue is common in calves in anterior presentation, in which the normal passage of the fetus is delayed and the head is retained for several hours in the birth canal or protruding through the vulva. This edema of the tongue and often of the entire head is due to passive congestion caused by the intrapelvic pressure exerted on the calf's neck interfering with or blocking venous circulation from the head. Edema of the forelimbs is observed frequently in prolonged dystocia when the forelimbs are extended so the fetlocks are outside the vulva. If the young is still alive the edema disappears within 3 to 24 hours after birth and the fetus can then suckle in a normal manner.

Intertwined or twisted umbilical cords and straw in the nest of kittens may result in their starvation and death due to inability to move about freely. Occasionally the umbilical cord looped around a kitten's leg may cause a slough. This may be due to the queen not properly cleaning the kitten and eating the long umbilical cord.

Injury or death of the newborn caused by the dam— Occasionally the dam, usually a primiparous female, may become excited, belligerent, or vicious, and injure or destroy the young soon after birth. This is a further reason for having a quiet environment to which the animal is accustomed, and an attendant present during parturition. It occurs rarely in the cow or mare but is seen occasionally in sow and bitch. When the cow attacks, butts or kicks its calf, the calf should be removed or the cow restrained or tranquilized until it becomes reconciled to and accepts the calf. In a few mares colic associated with uterine involution and expulsion of the fetal membranes may be quite severe. A sedative or tranquilizer is indicated and in some instances the foal should be removed from the stall for several hours to prevent accidental injury by the dam. Occasionally a mare will refuse to allow a colt to nurse and kicks him away from her flank. The mare-foal bond is established at birth by appearance, sound and smell. The latter comes from the fetal fluids. If the dam is highly nervous or exhausted from a painful or difficult birth and this bond does not occur soon after birth, it may not develop.^{55a} This calls for restraint and tranquilization of the mare at regular intervals even to an attendant employing a twitch to allow the foal to nurse. Between nursings the foal should be confined in a partitioned part of the box stall. The dam may accept the foal after 1 to 2 days when the congestion and soreness has left her udder.

In swine this viciousness may be marked and the primiparous or young sow will attack and kill her offspring. About one percent of the pigs farrowed in Iowa, Illinois, and Indiana are eaten by sows.⁶³ The sow may kill her

pigs as they are farrowed or farrowing may be normal and then the sow kills the entire litter at one time. Some pigs are eaten but most are merely killed thus this condition is not a true "cannibalism." This condition rarely occurs after 24 hours after farrowing. The "berserk" sow may even attack the owner. Obviously it is necessary to have this type of sow farrow in a farrowing crate or for the attendant to remove the pigs immediately after birth. Nutrition as a cause of this condition is doubtful since usually only one sow in a drove fed the same ration is affected. It may be due to an inherited or congenital excitability, psychosis, or viciousness. Gilts from affected or related sows may also develop a similar aggressive attitude after farrowing. The hereditary or genetic nature of this condition has not been proven but seems more likely than the nutritional theory as the cause of this condition. Quiet sows and gilts should be selected for breeding.

In order to attempt to induce this type of sow to accept her pigs the surroundings should be quiet. Some owners and veterinarians truss the sow up and allow the pigs to nurse at regular intervals. Spontaneous recovery may occur at any time. Often the sow is given a sedative or narcotic dose of chloral hydrate, pentobarbital or other strong sedative before the pigs are placed on her.⁶³ Along with this, some veterinarians advise the injection of 2 to 5 ml., or 20 to 50 units, of oxytocin, but its value is questionable. The sow and her pigs should be closely watched, since as soon as they regain consciousness some sows will again attack their pigs. If this viciousness is pronounced and the sow refuses to accept her pigs in 1 to 2 days they should be placed on other dams or hand fed. Treatment frequently fails. This undesirable inherent disposition was aggravated by parturition. This type of sow is usually sent to slaughter.

The same condition is also observed in bitches, especially Cocker Spaniels, and rarely in queens after parturition. Occasionally the dam, especially in primipara, will totally reject her offspring and not clean or nurse them. Their surviving offspring usually have to be reared as orphans.^{46,52} Animals should not be reared from such unstable psychotic dams for fear of perpetuating such individuals.

Care of the Postpartum Dam—Following parturition the dam should be allowed to lick and nurse her young. All undue excitement, noise, or unusual happenings should be eliminated or prevented. Rest and quiet following parturition is imperative. The roughage fed to large animals should be of good quality. The grain ration should be rather laxative and light, such as bran, oats, and a little linseed meal. In most animals the amount of grain should be increased gradually during the first three weeks after parturition. In the dairy cow it may have to

be increased more rapidly, to prevent ketosis. In the sow the light grain feed should be continued for a week and then gradually increased. If it is increased too rapidly the pigs may get too much milk, and diarrhea may develop. In the mare a bran mash or two following foaling may be of value if the mare is constipated. Some veterinarians routinely administer one gallon of mineral oil to mares soon after foaling to help prevent constipation due to the pain occasioned by the act of defecation the first few days after foaling. Milk yield in mares, as in cows, was maximal, 11.8 kg., at 30 days postpartum and declined to 9.8 kg. in late lactation.^{47b} The cow should be watched carefully for several days after calving for symptoms of milk fever. Excess edema of the udder should be controlled by massage, frequent milking, or preferably diuretics such as the carbonic anhydrase inhibitors with or without the glucocorticoids as described under lactation. Udder suspensories may be indicated in some cows to help support the edematous udder. Although urticaria due to the absorption of milk proteins into a sensitized animal occurs most commonly at the time of drying off, especially in Guernsey and Jerseys, it may occasionally develop after parturition if milking is limited in order to prevent the occurrence of milk fever. In most animals it takes about 10 to 14 days to return the dam to full feed. Moderate and light daily exercise is advisable in animals after parturition. Mares should be turned out for about one hour a day for the first week and then for longer periods thereafter. Draft or saddle mares can begin light work in two weeks.

In domestic animals retention of the fetal membranes occasionally occurs. The membranes are considered as being retained if they are not expelled within 8 to 12 hours in the cow, 3 to 6 hours in the mare, and 8 to 12 hours in the ewe. Retained placenta occurred twice as frequently in cattle when the calf died at birth than in normal parturitions and these cows had a lower conception rate.¹¹³ In multipara, membranes usually cannot be observed hanging from the vulva and they frequently go unnoticed until they are expelled in 1 to 2 days or decompose and a mucopurulent discharge is noted in 4 to 10 days. It is desirable, especially in the cow and mare—in which species retained placenta occurs most commonly—to have this condition treated by a veterinarian. Veterinarians prefer to treat retained placenta in the cow within 1 to 3 days after parturition. Mares should be treated earlier, within 12 to 24 hours, to avoid septicemia, toxemia, and possible parturient laminitis (See Chapter XI).

If genital discharges persist beyond 14 to 20 days postpartum or if they are abnormal in amount or purulent in nature, the genital tract of the animal should be examined and treated as described under uterine infections.

It is desirable especially in valuable cows to examine the genital tract about 30 days postpartum even when the calving and the postpartum period were apparently normal. In mares a vaginal examination and possible uterine culture should be made about 6 days postpartum if breeding is to be at the foal estrum, or early in the second estrum if the mare is to be bred at that estrum. Early treatment of uterine infections or pathology or repair of vulvar lacerations after parturition is essential if the animal is to conceive promptly.

Occasionally animals develop an acute septicemia from uterine or mammary infections within 24 to 48 hours postpartum. The symptoms may be severe and death result. The dam may be so severely affected that lactation is greatly suppressed and the young may perish or must be raised as orphans. Any illness occurring immediately after parturition should be treated promptly.

Agalactia, or a lack of milk after parturition, may be due to the failure of milk let-down or failure of milk production. In the former condition adrenalin, due to stimuli such as pain and fright, is thought to be secreted. This hormone antagonizes or prevents the let-down of milk by the posterior pituitary hormone, oxytocin. This condition is noticed occasionally in heifers with a greatly congested, edematous, painful udder; injections of pituitrin or oxytocin intravenously or intramuscularly cause rapid and complete milk let-down. Sometimes repeated injections at each milking are required. The failure of milk production, if not caused by diseases such as: acute metritis, acute or chronic mastitis, traumatic gastritis, indigestion and others, is due to a hormonal deficiency or to defective development of the mammary gland with a lack of secretory tissue. Prolactin from the anterior pituitary gland apparently is important in initiating lactation, while the growth or somatotrophic hormone is responsible for the maintenance of proper and high secretory levels. Injections of crude anterior pituitary extract have been used by veterinarians with questionable success as a possible aid in stimulating lactation. With the commercial production of the separate hormones of the anterior pituitary gland, such as prolactin and growth hormone, the therapy of these animals with low production of milk after parturition, may be improved in the future. Marked agalactia in sows and mares was associated with the feeding of ergot the last few weeks of pregnancy.¹⁰¹ Mortality in piglets due to starvation was high. At present the treatment or correction of severe agalactia is unsatisfactory and usually the newborn must be reared as orphans. In most cases with no obvious cause, rebreeding is questionable and affected food-producing animals should be slaughtered.

Occasionally it may be desirable to hasten mammary involution in animals that have lost their newborn young,

or in bitches in pseudopregnancy. Cessation of milking; application of mild liniments, such as camphorated oil, to the udder; withholding or drastically reducing water and TDN intake, and injections of estrogens, in larger animals at repeated intervals if necessary, are valuable in reducing udder size and suppressing milk secretion.

Care and Diseases of the Newborn Animal, Aftercare of the Dam

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Chapter VII

DYSTOCIA—ITS CAUSES

When the first, or especially the second, stages of parturition is markedly prolonged, becomes difficult or impossible for the dam without artificial aid, the condition is termed **dystocia**. The term dystocia comes from the Greek and means difficult birth. **Eutocia** is safe, easy, natural or physiological parturition. There is no clear line between normal parturition and dystocia. Dystocia is one of the most important obstetrical conditions with which the veterinarian must cope. Because of the many variable managerial and genetic components the incidence of dystocia in the various species is not satisfactorily recorded. Of the domestic species dystocia is most common in cattle, especially in primipara and in the larger breeds.^{1,11,28,29,37} The overall incidence of bovine dystocia ranges from 3 to 25 percent. Dystocia in beef cattle corrected by means other than cesarean section reduced their future reproductive performance 5 to 16 percent while in cases corrected by the latter operation it reduced performance 30 to 40 percent.^{8a} The incidence of dystocia in mares and sows is about 1 to possibly 2 percent and slightly higher in ewes due to twinning. In dogs it is highest in the Boston, Scotch Terrier, Pekinese, Sealyham, and other small brachycephalic breeds. It is lowest in the more natural breeds such as the hounds and mongrels. In queens the incidence of dystocia is probably slightly lower than in bitches. It is obvious that the incidence of dystocia is highest in the more specialized breeds and those kept under greatest confinement in the most artificial manner. Dystocia is much more common in primipara than in pluripara. The incidence of dystocia is greater in pregnancies that terminate early due to uterine disease, fetal death, and twinning, or that terminate after a prolonged gestation period due to excessive size of the fetus.

The causes of dystocia may be divided into the basic and the immediate causes. The basic causes should be studied for the purpose of obtaining knowledge that will help prevent the occurrence of dystocia. If basic causes are known and recognized, dystocia may largely be avoided; or if unavoidable the veterinarian and owner will know in advance that dystocia is highly probable. The latter circumstance requires certain preparations and precautions so that if dystocia should occur, prompt ob-

servance and handling may prevent injury or death of either or both the dam and fetus.

The Basic Causes of Dystocia

The basic causes of dystocia may be divided into the following categories: hereditary, nutritional and managerial, infectious, traumatic, miscellaneous, or combined causes. Many cases of dystocia may have two or more basic causes.

Hereditary Causes—The hereditary causes for dystocia may be divided into those that have produced defects in the dam which predispose to dystocia, or those hidden or recessive genes in the dam and sire which may produce a defective fetus.

Those hereditary defects in the dam predisposing to dystocia are inguinal hernia; persistence of the median wall of the Mullerian duct with a large band in, or caudal to, the external os of the cervix; double uterus or uterus didelphys; hypoplasia of the vagina or vulva, such as rectovaginal constriction in Jerseys, twinning; and inherited breed characteristics. Inguinal hernia as a cause of dystocia especially in the dog has been discussed previously. Persistence of the median wall of the Mullerian or paramesonephric duct may cause dystocia by obstructing the passage of the fetus if one leg should pass on one side and the other leg on the other side of this strong band. In a true double uterus in the cow the placental area is limited to only one horn. A severe dystocia may result from overlooking a twin in the other horn. Hypoplasia of hereditary origin is only rarely a cause for dystocia, as the hypoplasia often affects the uterus and ovaries, and conception does not occur. Twinning in uniparous animals is usually associated with double ovulation. Monozygous twins are uncommon. The release of two or more ova at one estrum is usually predisposed by the dam's hereditary constitution or may be associated with cystic ovaries in cows and the nutritional status of ewes. Twinning may be influenced to a lesser degree by the season and the age of the dam. Twin bicornual pregnancy in cows and ewes often results in dystocia because the long extremities frequently cause wedging

of the fetuses in the pelvis. In twinning, uterine inertia associated with unicornual twins, posterior presentation of one fetus, death of one or both fetuses, and premature twin birth or abortion also favor dystocia. Certain breeds of cattle, such as Brown Swiss and Charolais with a long gestation period and large fetuses; and certain brachycephalic or dwarf breeds of dogs, such as Bulldogs, and other breeds with a large, broad head and a relatively small pelvis and underdeveloped or weak reproductive systems, are more prone to dystocia. Scotch Terrier fetuses have a tendency toward premature hardening of the skull bones that may lead to dystocia. Most of the hereditary defects of the dam resulting in or predisposing to dystocia, with the possible exception of the inherited breed characteristics, are favored by inbreeding or close breeding practices.

The hidden and usually recessive genes in both male and female animals may produce a variety of pathological conditions affecting the fetus or fetal membranes, thus causing dystocia. Most of these are lethal genes, as they usually result in the death of the fetus. The known genetic lethals for cattle and the other domestic animals have been outlined in Chapter III. Dropsy of the fetal membranes and fetus may be caused by mating hybrids such as the bison with the domestic cow or zebu. Inbreeding in Dexter and Tux-Zillertaler cattle and others has resulted in **achondroplastic calves** and occasionally hydramnios. Certain types of muscle contracture monsters may be associated with hydrops of the amnion. If this condition should go to term it usually is associated with uterine inertia and a weak or dead fetus. Both of these conditions favor fetal emphysema and dystocia. Achondroplastic and "ankylosed" calves have been produced without dropsy of the fetal membranes by inbreeding animals with the recessive gene for those conditions. Dystocia often results at parturition due to the increased size of the fetus or certain of its parts. Hereditary lethals causing amputated limbs of fetuses, **Acroteriasis congenita**, **hydrocephalus**, and stillborn fetuses frequently may cause dystocia. Hydrocephalus in cattle is frequently associated with deformed limbs. The early death of these fetuses at the time of parturition, and abnormal postures more common in defective fetuses, increase the incidence of dystocia. An hereditary condition called congenital dropsy resulting in large, anasarctous fetuses or calves occasionally causes dystocia in Ayrshire or Swedish Lowland cattle when carried 200 days or longer. An autosomal recessive gene causing a **prolonged gestation** of 300 to 370 days in Holstein cattle and terminating in severe dystocia due to the oversized, giant calves has been described. In this case the fetuses were already dead, died at birth, or were killed during the difficult delivery. The dam's life was greatly imperiled and a

number of the dams died as a result of the dystocia. Mummified fetuses in cattle occasionally may be hereditary. Dystocia may result at the time the mummified fetus is expelled, especially in cases of fetuses that mummify after the fifth month of gestation. Muscular hypertrophy or "double muscling" in cattle is an hereditary condition that when present in fetuses, especially in primipara, often causes severe dystocia. Muscular hypertrophy has been described in Charolais, Holstein, South Devon, Hereford, Angus and Piedmont cattle. Fifty percent of oversized fetuses in Belgium causing dystocia were double-muscled.³³ Some of these lethal conditions causing dystocia affect bone development. The so-called muscle contracture monsters are usually produced by general functional ankylosis with an abnormal development of muscles and tendons, causing an immobility and extreme rigidity of the affected limbs. In sheep inherited lethals of general ankylosis and amputation and in swine general ankylosis have been described. There are many other inherited lethal genes such as cerebral hernia, epitheliogenesis imperfecta, and short spine that might contribute to dystocia because the fetus is weak and usually dies at the time of parturition. This factor of a dead or weak fetus at parturition favors abnormal postures of the fetus even though its size may be small, and its shape normal or nearly normal. A recessive hereditary condition should be suspected when several similar abnormal fetuses or dystocias are seen in related animals, over a period of several years.

Nutritional and Management Causes—The nutrition of a pregnant animal and its management at parturition are closely associated and may be the basic causes of many dystocias. Dystocia due to the small size of the dam is frequently observed in primipara. One study³ measured the area of the pelvic opening in 3-year-old heifers. As the pelvic opening increased in size from 200 sq. cm. to over 279 sq. cm. the incidence of heifers with a normal birth rose from 44 to 100 percent. Almost all severe dystocias were in heifers with pelvic areas of 200 to 240 sq. cm. or less. Improper nutrition of the growing heifers was the most important factor in retarding body and pelvic growth. This study was further confirmed by a similar one in younger heifers.²⁷ This condition may be caused by breeding the female at too young an age or by breeding a poorly grown, under-fed female that may be old enough to breed but the body growth has been greatly retarded due to poor nutrition, parasitism, or disease. Most domestic animals reach puberty before their body growth is great enough for a normal gestation and parturition. Dairy calves may show estrum at 3 to 12 months of age. Range calves still nursing their dams may occasionally come into estrum and be bred by a bull that is running with the herd. Many cases of severe dys-

tocia have been reported in cattle 13 to 18 months of age. Twenty-six percent of 2 year-old range heifers had dystocia as compared to 4 percent of the older cows.³¹

Well-grown, well-nourished heifers are usually not bred before 12 to 20 months of age, mares 3 years of age, gilts 6 to 8 months of age, ewes 1 to 1.5 years of age, and bitches 1 year of age. Dairy heifers should be bred by size or weight rather than age.⁷ Holstein or Brown Swiss heifers should be bred when they weigh 750 pounds; Ayrshire and Guernsey heifers when they weigh 600 pounds and Jerseys when they weigh 500 pounds. Depending on the levels of energy intake these weights may be reached from 10 to 19 months of age. The optimum feeding levels produce heifers of these weights from 13 to 17 months of age. During the gestation period animals should be fed sufficiently well to maintain their rate of growth so that at calving Holstein and Brown Swiss heifers weigh about 950 to 1000 pounds, Guernseys and Ayrshires 700 to 725 pounds and Jerseys 670 to 690 pounds. Restricting growth by underfeeding frequently results in dystocia and other periparturient difficulties. The breeding of animals that are immature or otherwise unfitted for a normal parturition is usually the result of an accident or gross carelessness in management. If discovered soon enough steps may be taken to prevent or terminate pregnancy.

Animals that are stunted frequently develop dystocia at parturition. This delayed development may be due to a low nutritive plane or to chronic diseases such as enteritis, pneumonia, severe pediculosis, mange or internal parasites. Stunting of a young female animal's growth is not permanent unless continued for a long period of time. In many young animals the stunting effects of a low plane of nutrition may be overcome by a high plane of nutrition for 6 months or more. Many farmers in dairy sections stunt the growth of their young stock by feeding milk substitutes improperly and by limited grain feeding, by feeding poor hay, pasturing the young stock on poor pastures, and by housing the young stock under unfavorable environmental conditions. Thus at the time of parturition the heifers are thin, small and weak. Dystocia is invited by the small pelvis and underdeveloped, juvenile genital tract, the lowered resistance to disease, and the lack of strength to expel the fetus in a normal manner. Growth and development in young animals should proceed normally from birth to puberty, from puberty to conception, and during the gestation period, if parturition is to be physiological. A proper nutritive level and efficient management are necessary to secure this goal.

High feeding levels may favor dystocia, especially in heifers, by excessive deposition of fat in the pelvic region, predisposing to difficult parturition. The influence

of over-and underfeeding of pregnant animals and its effect on increasing or decreasing the weight of the newborn has been demonstrated.¹⁸ Many owners try to compensate for low levels of feeding and poor growth in their young stock by high feeding levels during the last third of pregnancy. This is particularly true in dairy cattle, in which lactation is of major importance. This practice is of questionable value and may even be harmful, as it is during this last third of pregnancy that the fetus grows rapidly and the high feeding levels may favor the development of a larger fetus while increase in body size and growth of the immature dam occurs much more slowly. The balance between fetal size and pelvic or genital tract diameters, fetopelvic disproportion, and dystocia is favored. Overly fat, under-exercised sows and bitches often develop dystocia possibly due to uterine inertia.

Fetopelvic disproportion caused by the large size and weight of the fetus or the small size of the pelvis of the dam or both are the two greatest factors in dystocia of animals, especially beef cattle. Sires, especially those bred to young immature dams should be selected for the ease of birth of their offspring.^{21b} Male calves because of their larger size, partly due to their slightly longer gestation period, are most often associated with dystocia. Immature females should be managed and fed so that at the time of breeding and parturition they are healthy, not overly fat or thin, are of sufficient size and with a pelvic area large enough to give birth without assistance.^{4b,37b}

Failure to keep animals approaching or beginning parturition under close observation may not actually be a cause of dystocia but this neglect may cause a relatively early and simple dystocia to become more severe, with danger to the life of the fetus and the dam. During parturition all animals should be watched closely but not disturbed. No reliable birth detection system has been developed (see Parturition). Prompt aid may thus be given if parturition is not normal. This aid may prevent secondary uterine inertia, death of the fetus, rupture of the uterus or birth canal, fetal emphysema, septic metritis, retained placenta, and injuries, such as obturator paralysis. Feeding or grazing pregnant animals on plants that may damage the fetus such as ewes on *Veratrum*, should be prevented in an effort to control fetal losses and dystocia that may accompany such losses.

Pregnant animals which are not exercised and are kept in close confinement are more prone to difficulties such as torsion of the uterus and uterine inertia than those kept under more natural conditions, as on pasture. Exercise increases body tone, strength, and resistance and results in stronger labor contractions, less fatigue, shorter duration of parturition, less uterine inertia, and more prompt

recovery. Pregnant animals closely confined for long periods are more prone to abnormalities in the function of smooth muscle including prolapse of the vagina and uterus, intussusception, torsion of the cecum and displacement of the abomasum. In the first stage of labor the limbs of uniparous animals are flexed while during the second stage of labor they are extended. The strong contractions of the myometrium initiated active fetal movements and righting reflexes resulting in extension of the limbs.¹ Thus uterine disease as well as fetal disease may greatly influence the incidence of dystocia.³⁷

Infectious Causes—Any infection or disease affecting the pregnant uterus and its contents may cause abortion, uterine inertia, fetal death, and occasionally septic metritis of pregnancy. In any severe infection of the uterus the uterine wall may lose its tone or ability to contract—a condition resulting in incomplete dilation of the cervix and uterine inertia. In the latter instance the second stage of labor may be abnormally delayed. Death of the fetus prior to parturition or premature birth renders the fetal extremities prone to postural abnormalities, and may result in a dorso-pubic position of the fetus in the mare. The relation of uterine disease to hydrops of the allantois and edema of the fetus has been cited and may be a cause for uterine inertia and dystocia. Infections may be the immediate cause of conditions that predispose to dystocia, or they may be responsible for chronic uterine damage such as loss of caruncles, or a nonfunctional uterine horn, either of which may result in abortion, uterine inertia, hydrops, torsion, rare transverse pregnancies, and other abnormalities at subsequent pregnancies. All known infectious reproductive diseases such as brucellosis, leptospirosis, vibriosis, salmonella, viral, and other septicemic or infectious diseases should be controlled according to our best knowledge at the present time so that late abortions or premature births, in which dystocia is common, will be kept at a minimum.

Traumatic Causes—Traumatic causes for dystocia are not common. Ventral hernia and rupture of the prepubic tendon late in gestation may occur from traumatic causes. These injuries predispose to dystocia by rendering the abdominal wall incapable of strong contractions, with a resulting inability of the dam to force the fetus through the birth canal. Torsion of the uterus may be caused by sudden slipping, falling, or rolling in advanced pregnancy. This is not the only factor but it is an important one in the etiology of torsion. Fractures of the pelvis with secondary deformity and exostoses is seen most commonly in small animals struck by motor vehicles. These may result in a stenosis of the birth passage, resulting in a severe dystocia.

Miscellaneous Causes—The causes of certain minor

abnormalities in posture, such as a flexed knee or lateral deviation of the head and neck, resulting in dystocia with a live fetus and an apparently normal uterus, are difficult to explain except as an accidental catching of the nose or foot on the brim of the pelvis or in the soft structures of the birth canal during the early stages of parturition. A degree of uterine inertia or disease of the fetus may also be important factors. As the second stage progresses and more of the fetus enters the birth canal the deflection of the extremity is further increased. The causes of posterior presentation of the fetus, a relatively common cause for dystocia in uniparous animals, have not been satisfactorily explained. The exact causes or even satisfactory theories are not given to explain transverse pregnancies in domestic animals. Previous uterine disease in mares may predispose to transverse pregnancy and dystocia.³⁷ However another worker disagreed and reported that in 11 cases of bicornual pregnancy in mares there was no previous history of uterine disease.³⁴ In multipara a fetus may be located transversely in the uterine body, with the two ends of its body in separate horns. This may occur in polytocous dams having only a single fetus or it may be due to a fetus being misdirected during birth into the opposite horn rather than the vagina. In multipara with only about one-third the normal-sized litter the fetuses are often larger than normal due to increased nutrition and available uterine space. This may result in dystocia at parturition. In swine the most important factor determining the birth weight of pigs was the number of pigs in a litter, the larger the litter the smaller the pigs.¹⁸ Improper hormone balance of estrogens, progesterone or relaxin, or failure of the normal release of oxytocin may result in delay of the first stage or second stage of parturition, and in uterine inertia.²⁴

Uterine Inertia is defined as the lack of normal physiologic uterine contractions during or after parturition. Two types of uterine inertia are recognized, primary and secondary. **Primary uterine inertia** is seen most often in the bitch, occasionally in the cow and sow and rarely in the mare or ewe. The following conditions may be factors causing primary inertia or lack of uterine tone and feeble contractions at the time of parturition. It is observed more often in animals that are closely confined and hence lack exercise. It is more common in dairy than beef cattle. Obesity may be a possible factor in bitches and other species. Certain brachycephalic breeds of dogs tend to develop uterine inertia despite the size of the litter.^{15,16} Overstretching or overloading of the uterus in hydrops and twin pregnancy in cows, and a large number of fetuses in small bitches and sows may predispose to uterine inertia. It is observed more often in older dairy cows and bitches. It is frequently associated with nutri-

tional debility or debilitating diseases. It may be associated with disease or degeneration of the uterine wall due to uterine infections or secondary to peritonitis such as traumatic peritonitis. It may be associated with an improper hormonal balance during the complex process of parturition or the response of the genital tract to the various hormones. Further studies in this important area are needed. A primary uterine inertia in dogs associated with a small number of fetuses where symptoms of parturition are absent and the fetuses die has been described.⁶ This is probably due to a hormonal disfunction. A combination of the above factors may be present.

Secondary uterine inertia, which is seen in all species, is the result of or follows dystocia and is due to exhaustion of the uterine muscle. In multiparous animals it may follow dystocia with one fetus; the remaining fetuses may not be expelled when the fetus causing the dystocia has been removed. Certain "sensitive" dams will refrain from vigorous labor because of apparent pain or discomfort and secondary inertia may ensue. In other multiparous animals lacking body condition or strength several young may be born and then the dam and also the myometrium appears exhausted. After several hours rest the birth process will again proceed or may fail and outside aid will be necessary. Secondary inertia is frequently followed by uterine infection, septic metritis, retained placenta, and a failure of the normal involution of the uterus. In prolonged dystocia in unipara and possibly multipara, the uterine muscle may become fatigued and produce contraction or retraction rings, also called Bandl's rings, that contract tightly around the fetus or caudal to it. This may further complicate the relief of the dystocia or if not recognized it may result in rupture of the uterus if forced extraction is applied to the fetus. A condition in bitches—especially Scotch Terriers and toy Dachshunds and sows is described that is intermediate in character between primary and secondary uterine inertia.^{6,28} In these cases the bitch may have 1 or 2 fetuses and then labor ceases with a number of fetuses still in the uterus. There is no apparent cause for the dystocia. Many cases of secondary uterine inertia may be avoided by careful observation of the female during parturition so that proper help can be given as soon as difficulty arises.

Fetal monsters other than those described under hereditary causes for dystocia are considered accidental occurrences at the present time. Many of these are double monsters, with doubling of parts or nearly all of the fetus. These double monsters apparently arise from incomplete development or separation of monozygotic twins in the early embryonic period. Single fetal monsters may have a portion of the fetus that is too large to readily

pass through the birth canal. Since these more extreme monsters occur sporadically as a cause for dystocia and since their origin is so early in the gestation period little is known of their basic causes.

During the past 10 to 20 years many studies have been conducted on dystocia or calving difficulties in dairy and especially beef cattle because of the large economic losses in calves, cows, labor and infertility or delayed rebreeding produced by such difficulties. Although similar extensive studies on the other species of domestic animals have not been conducted, probably because the incidence of dystocia in these animals is much lower than in cattle, there are common significant correlations and observations that apply to all species.^{1,11,20,21,23,26,29}

Fetopelvic disproportion is the most common cause of dystocia in cattle, particularly in primipara beef cattle. About 30 percent of all bovine dystocias are due to this cause, with an incidence of 50 to 75 percent in beef cattle and 15 to 30 percent in dairy cattle.^{29,32} In beef cattle practice in the midwest U.S. about 90 percent of dystocias are due to fetopelvic disproportion.² The occurrence of dystocia is primarily related to the size or weight of the fetus and the pelvic area of the dam.

Fetal size, weight and conformation are dependent on: **Genetic factors** including sex—male calves at birth are 4 to 6 more pounds heavier and have larger body measurements of heart girth, pelvis width and length and head width.²⁶

Length of gestation—this is a function of the genotype of the fetus. Male fetuses are carried several days longer than female calves and both the sire and dam contribute to the length of gestation. A positive correlation between gestation length and birth weight of the calf exists. The larger breeds have a longer gestation period.²⁶

Breed or genotype of sire and dam—both parents contribute significantly to the size or weight of the fetus, dystocia and resulting calf mortality especially in heifers. Calves sired by the large breeds, Charolais, Simmental, Limousin, South Devon, Holstein and Brown Swiss bulls were larger and heavier than calves sired by the small breeds, Angus, Jersey and Hereford bulls.^{1,26,29} Heterosis or crossbreeding also contributes to increased calf birth weights. Conversely inbreeding, especially at high levels, decreases calf birth weight and also increases dystocia and calf mortality.²⁶ Even within a breed there are genetic differences between bulls in the transmission of size or weight and viability of the calf at birth. Many artificial insemination centers publish this information for bulls of the larger breeds so that farmers breeding heifers can select sires producing smaller calves and avoid sires producing large

calves.^{8b,c,9,23,25,32} This reduces calf mortality, calving costs, reproductive failures and generation interval. Another genetic trait of double muscling seen in the beef breeds affects the conformation of the fetus and often results in severe dystocia even though the weight of the fetus is average. However crossbreeding between mature Jersey or Guernsey cows and Charolais or double-muscled bulls resulted in only a slight increase in dystocia.^{19,22} Thus genetic effects between certain breeds crosses seem less hazardous **and non-genetic factors** including **age of dam or degree of maturity** and growth are reflected in the size of the pelvis and genital tract. Evidence was cited to indicate that the incidence of dystocia in cattle under 2 years of age was over 70 percent, and this decreased to 66 percent in 2 year-old and 44 percent in 5 year-old primipara and to 13 to 20 percent in adult pluriparous cows.²⁹ Birth weight of Hereford and Holstein calves increased up to 7 or 8 years of age and then decreased slightly.²⁶

Nutrition—different levels of energy intake low, medium or high, for 90 days before calving affected calf weight with about a six pound differential between the low and high levels.²⁶ But there was no significant effect on dystocia.⁴ However excessively high energy intakes producing overly fat heifers caused an increased incidence of dystocia due to excess pelvic fat decreasing the size of the birth canal.^{23,29} Excessively restricted energy intake also resulted in an increased incidence of dystocia due to weakness and debility even though the fetus was not large.¹⁴ In the latter instance a delayed return to estrous cycling was a concurrent problem. Larger better grown heifers usually had larger pelvic areas but breed also had a significant effect on pelvic size. The larger the pelvic area the lower the occurrence of dystocia.^{20,21,26} With Hereford heifers with less than 200 cm² having a 69 percent incidence of dystocia, heifers with pelvic areas of 200 to 229 cm² and 230 to 269 cm² had a 30 and 25 percent incidence, respectively.

Miscellaneous factors—more dystocia is observed in the winter months possibly because the cows were in better condition in the summer or because more cows are confined and were observed and aided in calving in the winter.²⁵ Confined heifers had a higher incidence of dystocia and stillbirth, often characterized by vulvar constriction,¹² than did heifers in yards or paddocks. Possibly excessive disturbance during parturition influenced these results. Dystocia caused a 15 percent reduction in estrous recycling during the AI period postpartum and a 15 percent lower postpartum conception rate.²¹

Experiments using artificial insemination by which

Shire horses and Shetland ponies were mated to each other—Shire stallions on Shetland mares and Shetland stallions on Shire mares—proved that foals by a Shire stallion out of Shetland mares were not appreciably larger than pure Shetland foals.^{18,36} Foals by Shetland stallions out of Shire mares were three times as large as pure Shetland foals but not quite as large as pure Shire foals. This difference in size was greater in horses and less in the other species because the length of gestation in horses was longer and thus the influence of the maternal environment was greater. The foal is born in the most advanced state of physiological development while the pig is the most immature of the large domestic animals. At birth the foal weighs 9 percent and the pig less than 1 percent of their mature weight.¹⁸

The basic causes for dystocia are multiple, but by properly applying our knowledge its incidence may be kept at a minimum. In general all elements that lower resistance or otherwise unfavorably affect the general health and vigor of the dam or fetus increase the possibility of dystocia.

The Immediate Causes of Dystocia

Attendant upon dystocia are many forms of interference with physiological birth. The veterinarian handling dystocia is largely concerned with correcting or relieving the immediate interferences to birth, which may be divided for convenience into maternal and fetal types of dystocia; some overlapping may occur in certain conditions. In 95 cases of dystocia in cattle 25 percent were due to maternal causes and 75 percent due to fetal causes.³⁹ In 60 dystocia cases in goats 28 percent were maternal and 75 percent were fetal causes.^{27a}

The Maternal Causes of dystocia are largely those factors that produce a narrowing or stenosis of the birth passage or prevent the normal entrance of the fetus into the birth canal. These include: fractures and exostoses of the pelvis; small size of the pelvis due to breeding at too young an age, or due to improper rearing with resultant stunting of body growth; hereditary or congenital hypoplasia of the birth canal or vulva; compression or stenosis of the cervix, vagina, or vulva by indurations caused by scars and connective tissue usually from injuries at previous parturitions; intrapelvic hemorrhage; excessive perivaginal fat; impaction of the colon or distension of the bladder in bitches and sows; tumors such as chondrosarcoma of the pelvic bones, fibromas, lipomas or leiomyomas of the uterus, cervix or vagina, or lymphomas of the large pelvic lymph glands; torsion of the uterus; folding of the uterus just cranial to the pelvic brim, especially in deep bodied older sows;²⁸ persistence

of the medial wall of the Mullerian duct; failure of the cervix to dilate or "ringwomb" in ewes; uterine inertia; hydrops of the fetal membranes, inguinal, diaphragmatic or ventral hernias; rupture of the prepubic tendon; transverse presentations; uterine infections resulting in uterine inertia, death, abortion, or emphysema of the fetus; and twinning. In uniparous animals twinning is considered a maternal cause for dystocia since it is usually due to double ovulation.

The Fetal Causes of dystocia are more numerous and are due in general to abnormal presentation, position and posture and to excessive size of the fetus. (See Figure 86.) These include: certain posterior longitudinal presentations in uniparous animals and all transverse ventral and dorsal presentations; dorso-ilial or dorso-pubic positions; flexion of the limbs beneath the fetal body in unipara and in large fetuses in multipara; ventral, lateral or dorsal flexing of the head and neck; fetal anasarca, ascites, large fetal tumors, distention of any hollow organ such as the brain, liver^{11b} stomach, cutaneous sac in **Schistosomus reflexus**, kidneys and ureters; fetal giantism in prolonged gestation; and fetal abnormalities or monsters such as mummified fetus, general ankylosis, double monsters, achondroplastic fetuses, and others.

The incidence of dystocia in posterior presentations of the fetus in unipara is high. In 800 births in Holsteins 4.5 percent were posterior presentations but 47.2 percent of these were accompanied by dystocia.⁵ A Hereford sire used on an inbred line of cattle produced a high incidence of posterior presentations suggestive of an hereditary factor conditioning such a malpresentation.³⁸ Up to 30 percent or more of the fetuses in multipara are commonly expelled in posterior presentation without dystocia occurring. Some equine fetuses in longitudinal presentations may develop a wry or ankylosed neck.³⁴ It is possible but unlikely that an equine fetus that developed transversely in both uterine horns might rotate into a longitudinal presentation. If a fetus is presented in a dorso-ilial or dorso-pubic position, torsion of the uterus may be present. Many of the abnormal postures resulting in dystocia undoubtedly arise during the first and second stages of labor, with the fetal extremities catching on the pelvic brim or soft structures in the birth canal. These abnormal postures may often be predisposed by a weak or dead fetus.⁶ Lateral deviation of the head and neck is seen occasionally in all species except swine.

The Common Forms of Dystocia in Domestic Animals

In the mare dystocia is most often caused by an abnormal presentation, position or posture. The long ex-

trémities of the fetus tend to predispose the mare to dystocia. Abnormal posture of the head and neck is one of the most common causes of dystocia in mares. At birth the equine foreleg from the fetlock to the elbow is 73 percent of its adult length.¹⁸ Dystocia due to monsters or to disproportion between fetal size and pelvic diameters is rare. Transverse ventral presentation is not uncommon, whereas transverse dorsal and rotated bicornual or transverse pregnancies are very unusual. (See Figure 86.) The ratio of transverse to longitudinal presentations in mares at foaling was 1:1000.³⁴ Dorso-ilial or dorso-pubic positions are occasionally found in the mare due to the fetus failing to rotate into the normal dorso-sacral position early in parturition. All forms of abnormal posture may occur in the mare. One or both of the long forelimbs may become lodged over the neck of the fetus. Wry neck is seen most commonly in the equine fetus which may or may not be associated with transverse pregnancy. Wry neck is characterized by an ankylosis and atrophy and contraction of the neck muscles, thus causing the head and neck to be fixed in a lateral direction alongside the body, similar to a severe, long-standing case of torticollis. It cannot be straightened even after the fetus is delivered. The abnormal positions and postures, together with violent labor contractions, frequently result in wedging of the fetus in the pelvis or in laceration of the vagina, rectum or vulva. Only a very small percentage of equine abortions are due to maternal causes such as torsion of the uterus.³⁴

In the cow disproportion between the fetal size and pelvic diameters are common, especially in primipara.¹ Fetal giantism, hydrops of the fetal membranes and fetus, and fetal emphysema are not uncommon. The incidence of monsters such as achondroplastic fetuses, **Schistosomus reflexus**, **Perosomus elumbis**, double monsters and fetuses with general ankyloses is higher than in other species. Transverse pregnancy is rare. Uterine inertia and failure of the cervix to dilate are occasionally noted. Twin dystocia and dystocia due to uterine torsion are common. Breech presentation, lateral deviation of the head and neck, and postural abnormalities of the limbs are often observed.

In the ewe and doe postural abnormalities and twin or triplet dystocias are common. Marked disproportion between fetal size and pelvic diameters are uncommon. About 70 percent of Romney ewes delivering lambs weighing over 10 pounds had dystocia.³⁰ Fetal anasarca or emphysema are occasionally seen. Relative oversize of the head is seen as a cause for dystocia in certain crosses in sheep.¹ In 50 cases of dystocia in goats 7 were triplet and 21 were twin births; 3.5 percent were in transverse presentation, 15.3 percent in posterior and 81.2 percent in anterior presentation. In the anterior presen-

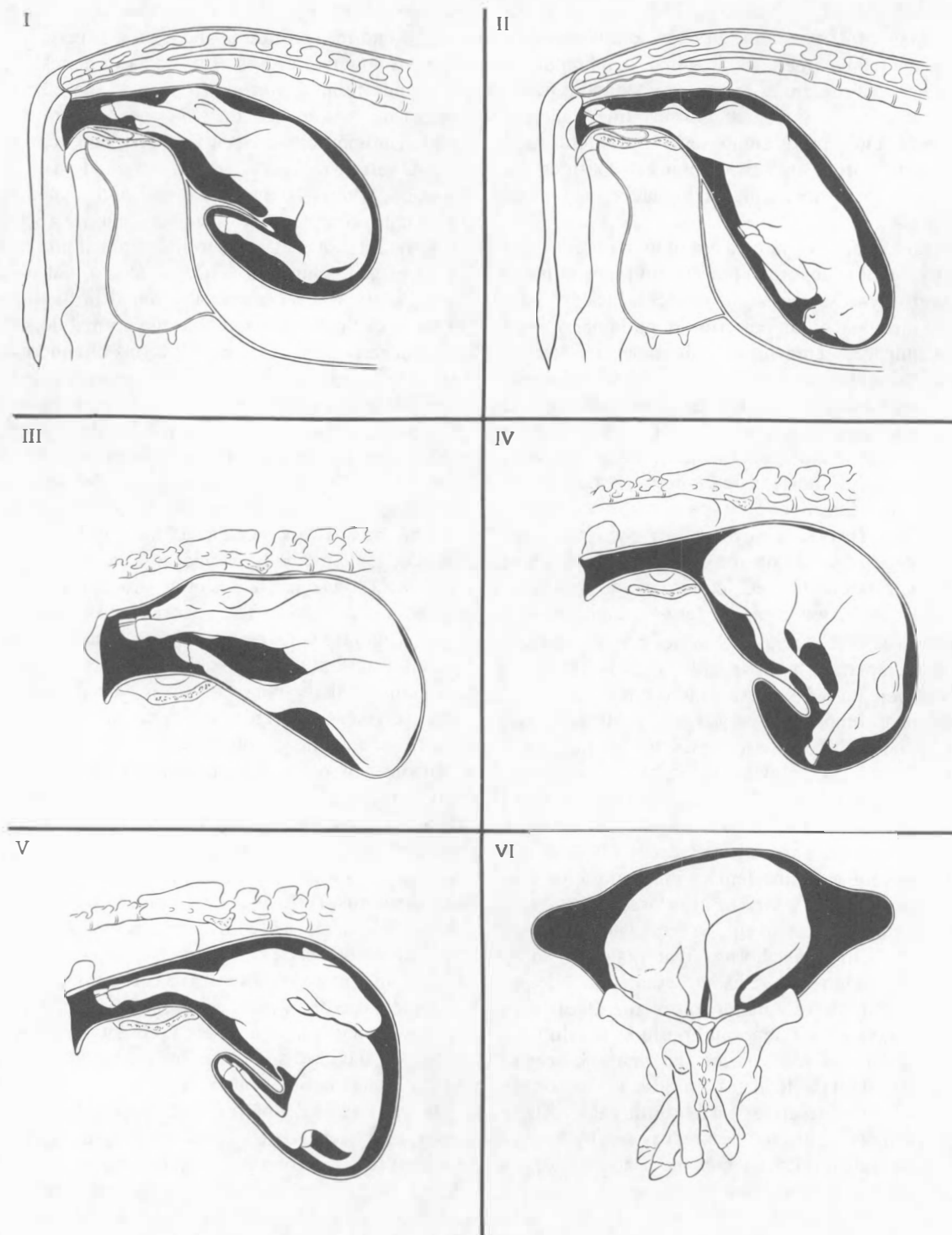


Figure 86. Normal and abnormal presentations, positions and posture in bovine and equine births. I Normal anterior presentation, II Posterior presentation, III Anterior presentation with the rear legs extended beneath the fetus ("dogsitting" posture), IV Posterior presentation with the rear limbs extended beneath the fetus (breech presentation), V Anterior presentation with the head and neck extended over the fetus, VI Transverse ventral presentation of a foal. (as adapted from Diseases of Cattle U.S.D.A., 1942, Harm's Textbook of Veterinary Obstetrics, and Veterinary Obstetrics, 2nd Ed., G. H. Arthur).

tation 31.5 percent had a deviated head and neck. In posterior presentations 80 percent of the single births had one or both hind limbs flexed.⁴⁰ In 1200 dystocias in ewes 65 percent of the fetuses were in anterior presentation, many with a lateral deviation of the head or with one or both forelegs flexed; 27 percent were in posterior presentation and two-thirds of these were in breech presentation; and 8 percent were in a transverse dorsal presentation. Failure of the cervix to dilate occurred in 15 percent of the cases.^{13,17}

In the sow the incidence of dystocia caused by uterine inertia is about 40 percent.²⁸ Small litter size tends to cause larger fetuses that may predispose to dystocia. Dystocia in immature or poorly grown gilts is occasionally observed. Abnormal fetuses such as cyclops and hermaphrodites are uncommon and seldom cause dystocia. Double monsters and hydrocephalus are rare, about 0.5 percent.²⁸ Stillbirths are high in sows with dystocia.¹ (See Figure 46.)

In the bitch disproportion between fetal size and pelvic diameters is common in toy and achondroplastic breeds. In the latter the large size of the head is the principal cause of the dystocia. Oversized fetuses are occasionally seen when there are only one or two fetuses.¹ Uterine inertia, either primary or secondary, is a frequent cause of canine dystocia. Nervous voluntary inhibition of parturition may occur due to excitement, a strange environment or pain.¹⁶ A prolonged first stage of birth may occur in posterior presentation of the first fetus because of failure of the head to engage in the pelvis and stimulate uterine and abdominal contractions.¹⁵ Poll presentation and lateral deviation of the head and neck are causes of dystocia. Postural abnormalities of the limbs are of little importance. Dorso-ilial and especially dorso-pubic positions are seen as a cause of dystocia. Monsters are rare except for occasional cases of hydrocephalus.¹⁶ Transverse presentation is rare and usually occurs only with bicornual pregnancy with a single fetus. A complete review of the causes of canine dystocia have been listed.^{6b}

In the queen dystocia may be due to postural abnormalities of the head and neck and to breech presentation. Only rarely are two fetuses wedged in the pelvis. Uterine inertia, hydrocephalus and a large calvarium in primiparous Persians have also caused dystocia.¹⁰

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Chapter VIII

PROCEDURES PRELIMINARY TO THE HANDLING OF DYSTOCIA

Dystocia cases are handled promptly as emergency calls but it is essential to a successful outcome that the animal be given a routine careful examination to establish the correct diagnosis so that a sound course of action can be outlined.

The History of the Case

As the preliminary examinations and preparations for handling the dystocia are being made, the history of the case as well as certain other information should be obtained from the owner or by observation. This information should include: the age of the female; the breed or information on the sire of the fetus; the dates of service and the duration of gestation; the previous breeding history; whether dystocia or any other abnormal condition was present at previous parturitions; whether the animal had exhibited any illness or unusual symptoms during the two months to the last few hours prior to parturition; the length of time the animal has been acting uneasy and shown anorexia or restlessness, or the length of time the animal has been in active labor. What is the nature of the straining—strong or weak, intermittent or regular, increasing or decreasing in frequency? Has the allantoic sac ruptured, the amnionic sac appeared at the vulva, or has any portion of the fetus appeared? In multipara have any fetuses been expelled and if so were they living or dead? Has any assistance such as traction been used by the owner, his neighbors, or even other veterinarians? Is the animal primiparous or pluriparous? Has the animal been able to get up if recumbent? This information is useful and necessary for the intelligent examination and handling of a dystocia case. The answers to some of these questions may have been obtained at the time the veterinarian was called or can be gotten along with the general examination of the patient.

The General Examination

The general examination of the patient with dystocia should include its physical condition, whether it is thin and emaciated, too fat, or in good condition. If the animal is recumbent the veterinarian should determine the

following: Is it able to rise or is it exhausted? If it is a heifer is it affected with obturator paralysis usually seen in hiplock conditions. In older dairy cows parturient paresis or other conditions causing paraplegia of pregnancy may be present. It is much better to diagnose the presence of such conditions as obturator paralysis and inform the owner before the operation. Afterwards, if this has not been done, the owner often will blame the veterinarian for having produced the paralysis during the relief of the dystocia. The pulse and temperature should be noted. In most dystocia cases the pulse is moderately elevated and the temperature may be slightly higher than normal due to the efforts at parturition. The degree of abdominal enlargement should be noted. Dystocia in dogs is often characterized by depression and futile laboring during which the bitch's mouth is open and its head is repeatedly thrown back. In exhausted prostrate animals the color of the mucous membranes should be noted for evidence of internal hemorrhage or shock due to rupture of the uterine vessels or rupture of the uterus. The general appearance and attitude of the animal should be observed, since some cattle affected with rabies frequently show tenesmus that might be confused with labor. Particular attention should be paid to the vulva. The nature of the vulvar discharge, whether it is watery, mucoid, bloody, or fetid will often indicate the condition of the fetus. If much fresh blood is present, injury to the birth canal has probably occurred due to the intervention of the owner or someone else. The character of the fetal membranes if hanging from the vulva are of further assistance in determining the condition of the fetus and the length of time the dystocia has existed. If a portion of the fetus protrudes from the vulva its condition and position and posture should be observed. The vulva itself should be noted to gain information on the amount of edema or trauma present as an indication of the length of time the dystocia has existed and whether someone has already been trying to deliver the fetus.

The Specific Examination and Restraint

The specific examination consisting of the detailed examination of the genital tract and fetus should be un-

undertaken only after the animal has been properly confined and restrained, as the obstetrical operations usually follow immediately after this examination.

If the animal is on pasture it is usually advisable, especially at night, in rough country, or during inclement weather to advise the owner, at the time he calls, to take the animal to a box stall in the barn, or to a shed near the dwelling house. This will usually insure light, easy access to hot water, and fairly comfortable working conditions. These are definitely desirable if a clean, careful obstetrical procedure is to be followed. It may avoid chilling and exposure of the operator as well as the patient. Aftercare and proper nursing are facilitated if the animal is near the owner's residence. A clean pasture lot or even a well-bedded stanchion stall are better locations in which to work than is a dirty, dark, cramped or too-small box stall. These suggestions are only common-sense practices and precautions but often if the veterinarian does not suggest or insist upon them the owner will neglect to provide satisfactory surroundings for the patient and operator. Working in the hot summer sun, on "the north-side of a barbed wire fence" in winter, knee-deep in water or filth, or in a dusty, dark, low swine house is not conducive to proper surgical cleanliness or technique. If a good supply of hot water is not available the veterinarian should take it with him.

If possible the animal should be standing at the time of the examination. A satisfactory examination and the handling of dystocia are much more difficult in the recumbent patient, with the viscera and fetus forced toward the pelvic cavity. Most animals rise promptly when urged. Others may be fatigued or may not wish to stand, and more vigorous methods are required such as; prodding them over the loins and rump with a sharp object, rolling the tail, sudden thumping of the ribs over the chest with the operator's knees, the use of the electric prod, or the intravenous injection of central nervous stimulants. Occasionally a cow which has refused to rise will do so after a small dose of anesthetic epidurally has relieved the pain. If the animal fails to get up, its rear parts should be raised above the front by lowering the front parts; or the rear parts may be placed on bags of straw, or elevated on a door or a plank resting on blocks and the animal held in place by a breast-harness. The rear parts may be hoisted by means of a figure-of-eight knot of rope around the hocks, which places the animal on its back, or by passing loops of rope around each leg up to the crotch and hoisting the animal's rear parts. If this latter method is used, the animal often falls sideways if it struggles. The judicious use of commercially available hip slings may be helpful in these cases. In nearly all cases of dystocia a standing position or the elevation of

the rear parts is necessary in order that the veterinarian may work with relative ease and effect a prompt correction of dystocia. It is therefore desirable that the animal be placed in this position prior to the examination.

The animals should be properly restrained so that they do not injure the operator at the time of the examination or operation. In mares a twitch usually should be applied to the lip and one foreleg held up. In range cattle a well-constructed chute is desirable, or cows might be fastened securely with a rope halter in a corner of a large box stall. If they kick, a nose lead will often divert their attention. In sheep the rear parts should be elevated by an assistant straddling the ewe. This position minimizes straining, aids repulsion and the introduction of a lubricant.⁶ Sows can be fastened securely by a strong rope with a loop around the upper jaw and behind the canine teeth. The sows may be secured or placed in a farrowing crate. Restless sows may be restrained by a short obstetrical chain around the metacarpus of the left foreleg and above the hock on the left rear leg and laying the sow on her left side.¹¹ Dogs should be muzzled or have their jaws tied together and cats should be held firmly by an assistant. The use of epidural anesthesia, tranquilizers or slight or deep narcosis may be necessary to properly restrain some animals.

In doing obstetrical work on large animals, the most satisfactory dress is: rubber boots, the type that slip on over the shoes; a pair of rubber pants or overalls; in warm weather a sleeveless cotton shirt or jacket and in cold weather a rubber jacket with no sleeves and the armholes cut or adjusted with elastic to fit tightly over the upper arm. Rubber or plastic gloves and sleeves can be worn, when indicated, to prevent infection and odors from contaminating the arms of the operator. These rubber or plastic gloves and sleeves are often damaged by instruments if fetotomy is employed. The long obstetrical gown is generally undesirable because it is extremely hot in the summer and does not provide proper protection to the lower portion of the operator's body when he has to kneel to work on the recumbent animal.

The animal's external genitalia and the surrounding structures should be washed thoroughly with warm water and soap. In sheep and long-haired dogs it is necessary to clip the wool and hair in the perineal area. The tail should be held to one side by an assistant or tied with a tail rope over the back to the opposite elbow. In the mare the tail should be bandaged or covered by a plastic sleeve. Adding a sanitizing detergent like the quaternary ammonium compounds and a wetting agent to the water used in washing the rear parts of the dam will aid in thoroughly cleansing the area. In cattle epidural anesthesia is helpful in preventing frequent defecation of loose

feces that contaminate the perineal area as well as the operator's arm. In some cases, however, epidural anesthesia might not be desirable, as it would cause a cessation of straining or labor. This straining may be helpful in the withdrawal of a normally-presented fetus. During the examination and obstetrical operation the perineal area should be kept washed and clean at all times. The operator should wash and lubricate his arms with water and soap or other nonirritating lubricant before making an examination of the birth canal and fetus. In the queen and bitch, after giving an enema and catheterizing the bladder, the rear parts may be cleansed and covered with a sterile drape; the veterinarian should wear sterile rubber gloves.

If the history of the case leads the veterinarian to know or suspect that others have been examining and attempting to relieve the dystocia, it is extremely important that the birth passages and caudal portions of the uterus be examined very carefully for evidence of trauma. In the middle of an obstetrical operation it is highly embarrassing to find a tear in the vagina or uterus which was present or had been produced before the operation was begun. If this injury causes the death of the animal, the owner might accuse the veterinarian of having injured the animal. The veterinarian would not be able to prove his innocence. The birth canal should be examined to see if it is dilated, twisted, moist or slippery, inflamed, swollen, dry, necrotic, contains pathological bands, stenotic areas or tumors, or contains gummy mucus indicating that parturition has not yet begun or is in the early stages. The degree of dilation or relaxation of the cervix should be noted as well as whether there is any evidence of torsion. The size of the pelvic inlet, vulva, and vagina in relation to the size of the fetus should be checked. Any other abnormalities of the birth canal should be noted. The canine or feline patient might benefit from radiography of the fetuses and pelvis of the dam to determine the fetal and pelvic sizes and if the fetuses are dead.^{7b}

The fetus should be examined to see if it is dead or alive as this will alter the prognosis and make a difference in the manner in which the case is handled. If the fetus is alive, grasping the foot and pulling or pinching it will cause movement of the limb. Pinching the eyeballs will cause the live fetus to shake its head. Placing the fingers in the mouth of the fetus may cause sucking or movements of the tongue and jaw. Putting fingers in the anus in breech presentation will cause contraction of the anal sphincter. If the fetus is dead the degree of decomposition or autolysis should be accurately assessed by the amount of subcutaneous edema or emphysema, whether or not the hair is sloughing and whether or not

a putrid, fetid odor is present. When fetal emphysema and sloughing of the hair is present the fetus has been dead for 24 to 48 hours or more depending on the degree of changes noted. After a dead fetus has been removed from the uterus, if no emphysema is present, the length of time death has existed may be approximately determined by the degree of cloudiness, turbidity or greying of the cornea. After the fetus has been dead 6 to 12 hours the corneas are grey and opaque.

The fetus should be carefully examined to determine any abnormality of presentation, position, and posture, or any teratologic defects. In a breech presentation the tail is often observed hanging from the vulva or lying in the birth canal. If the head is not in the birth canal in anterior presentation its location can be determined by finding the neck, the mane of the equine fetus, or the ears and head, by swinging the arm and hand around the cephalic part of the fetus. If the feet are lying in the birth canal it should be determined whether they are front or hind feet. Inexperienced students frequently confuse the front and hind legs by mistaking the hock for the elbow or the elbow for the hock. Front limbs have two joints, fetlock and knee, between the hoof and elbow, while hind limbs have only one joint, the fetlock, between the hoof and hock.

If the feet are protruding through the vulva with the soles ventral then the fetus is in either anterior longitudinal, dorso-sacral position or posterior longitudinal, dorso-pubic position. The latter rarely occurs. If the soles of the feet are dorsal then the fetus is in either posterior longitudinal presentation, dorso-sacral position; or anterior longitudinal presentation, dorso-pubic position. This latter condition is only rarely observed. In fetal monsters the differentiation into the various types may be quite difficult, as ankylosis and marked distortion are frequently present. Most of these abnormal fetuses have severely atrophied muscles of the limbs, making them feel thin, very firm, and rigid. If no part of the fetus is in the vagina of the mare the condition is probably a transverse dorsal or rotated bicornual pregnancy. In the latter condition the birth canal is very long and the fetus can be touched only at arm's length. Occasionally the amnion may not yet be ruptured, in which case if the birth passageway is dilated sufficiently the amnion may be ruptured with the fingers or a knife, so that palpation of the fetus may be facilitated. If more than two limbs are in, entering, or are near the pelvis, the condition should be examined carefully to differentiate between twins that are wedged in the pelvis, a *Schistosomus reflexus*, a double monster, an anterior presentation with the rear limbs of the fetus extended over or under the body, or in the mare a transverse ventral presentation.

It may occasionally be necessary to repel the fetus out of the birth canal and into the uterus in order to diagnose accurately the cause of the dystocia. If the animal is straining severely, epidural anesthesia should be given at once so that the examination can proceed without interruption. Sometimes examination is difficult, especially in a protracted dystocia in heifers, with swollen mucous membranes, a dry, dead fetus, and a uterus contracting tightly around it, making it impossible to repel the fetus. In mares and occasionally other animals, where the owner has applied traction, the fetus may become firmly wedged in the pelvis. A similar examination is made with a finger *per vaginam* in the bitch. Strict cleanliness is necessary, as in other species. If more than one fetus is palpated in the abdominal cavity and the bitch has suffered a prolonged dystocia, inertia has probably developed and cesarean section may be indicated. The importance of this complete examination cannot be overstressed, as it is the basis of the prognosis and procedures that follow in the handling of the case. It should be thorough and accurate to be professional, to save time and effort in useless and often harmful procedures, and to determine in severe cases whether or not outside help or consultation is needed.

Prognosis

The prognosis in dystocia varies widely between the different causes and species affected. For this reason the prognosis in the various types of dystocia will be considered as each type is discussed. In general the more prolonged the dystocia, the poorer the prognosis. The greater the trauma, irritation and infection of the birth canal caused by inexperienced laymen attempting to relieve the dystocia, the graver the prognosis. The prognosis in horses is graver than other domestic animals because the fetus usually dies within 30 to 40 minutes after the commencement of labor. The mare's pelvis is longer, and the fetal extremities are longer, making correction of the dystocia more difficult. Labor contractions are violent and powerful, predisposing to impaction of the fetus in the pelvis, lacerations of the birth passages or rupture of the uterine vessels. Lastly, the mare is more susceptible than other animals to trauma, irritation, infection, and inflammation of the birth passage and to peritonitis. It is difficult to save the life of a mare if she has been in labor for more than 24 hours and the fetus is emphysematous. The same is true of other animals but the prognosis is usually better, as other species are more resistant to infection. The fetus in the cow usually dies after 6 to 12 hours of labor and emphysema sets in about

24 to 36 hours after the onset of labor. In the bitch the first fetus usually dies within 6 to 8 hours³ after the onset of labor and may become emphysematous in 24 to 36 hours. But some of the other fetuses may still be alive. After 48 hours of labor no living canine fetuses are found. In sows the first pig usually dies after 4 to 6 hours of labor. The other pigs may survive for 24 hours. After 24 to 36 hours of labor all fetal pigs are invariably dead. The ewe is similar to the cow.

Williams very aptly described the handling of dystocia as resembling a salvaging operation on a "ship on the rocks." If it is possible, the following should be salvaged:¹⁵

1. the value of the surviving dam—its future breeding life, its food value for milk or meat, or its value for work.

2. the value of the newborn.

3. the sentimental value of the dam or newborn.

In the prognosis of a case of dystocia these values or credits should be weighed against the:

1. veterinary fees

2. mortality risk of the dam and the newborn

3. cost of labor and feed until the dam has recovered her value for milk, meat, work or breeding.

When these factors are considered and discussed with the owner after a careful examination of the patient, the prognosis and handling of the case will be understood by the owner. In the large farm animals whose value is usually entirely economic and not sentimental, the veterinary fees will then be paid more willingly. If the prognosis is correct these fees should not exceed the salvage or slaughter value. Many young veterinarians have labored diligently and corrected a severe dystocia, visited the animal several times subsequently to provide necessary care and drugs, and then presented the bill only to have the owner exclaim, "That's more than the heifer is worth." This embarrassing position would have been avoided if the above factors had been discussed fully with the owner before the veterinarian undertook the correction of the more severe dystocia cases. Thus the prognosis should take into consideration more than just the life of the dam or fetus unless the sentimental value is of prime importance.

Obstetrical Equipment and Anesthesia

The best guarantee of the proper and satisfactory handling of dystocia is the operator's correctly applied knowledge and experience. Good help and equipment may be available, but if the problem presented in each dystocia case cannot be perceived, the several methods

of handling it are not evaluated, a practical and logical approach and procedure are not developed, and the ability to follow the outlined procedure calmly and confidently to a successful termination are lacking, the case will probably end in failure, with a dissatisfied or disgusted owner. The best obstetrical equipment available should be used. Poor or makeshift equipment is not conducive to good surgical procedures. The instruments should be kept clean and sterile. Chrome or other types of plated or stainless steel instruments are desirable. During obstetrical operations surgical procedures of cleanliness should be followed in so far as this is possible. A plentiful supply of hot water, soap and lubricant are usually necessary. If possible a table should be provided and covered with a sterile sheet upon which the obstetrical instruments may be placed during the operation. Since this is usually lacking a clean pail of water to which an antiseptic has been added can be used and in which instruments may be placed or kept to prevent contamination. If the operation must be performed in a barn on a recumbent animal a sterile rubber sheet placed under the rear parts of the cow may help reduce contamination. In practice these sheets are difficult to hold in place. Epidural anesthesia may be necessary to control defecation. If the surroundings are poor the animal should be moved to a more suitable place.

It is not necessary to have all of the following obstetrical equipment for the handling of dystocias. Certain veterinarians become quite adept at using particular instruments while others prefer different ones. The type of practice in the various areas of the country also determines to a large extent the type of equipment that is accepted and used (see Figure 87).

Obstetrical Instruments for Traction on the fetus include:

Chains and handles: Gibbons' handles, while more bulky than the smaller Muir's handles, are better as they provide a longer, wider hand hold and do not cut into the hands. Obstetrical chains are preferred to sash cord or baling twine because they may be recleaned and sterilized, provide easier attachment for handles than does cord or twine. They are more professional in appearance. Obstetrical chains are strong, easily applied, and do not cause injury to the fetus or the genital tract of the dam. They are made in 10-, 21-, 30-, and 60-inch lengths. Lengths of 1- or 2-inch wide sterile gauze may be used for traction in dogs and cats.

Hooks may be long or short but should always be blunt. Sharp hooks are frequently the cause of injury either of the operator or the dam. Blunt hooks can do anything sharp hooks can, but without the added danger. The short hooks have an eye at their base, through which a cord

is run. The long hooks have a handle on the end opposite the hook. In general the long hooks are easier to apply because they can be turned or pushed from outside the vulva, but they occupy slightly more room than do the short hooks. The hook should be at a 45° angle from the shaft so that when traction is applied the hook tends to sink deeper into the fetal tissues. Another hook that is useful is Krey's hook or tongs. These may readily be applied to the orbits or other portions of a fetus when traction is desired during fetotomy operations. Krey's hook does not require guarding with the hands, as do other hooks that might pull out of the fetus and injure the birth canal or uterus.

A **fetal extractor** consisting of a mechanical hoisting or jacking device on the end of a long metal rod fitted into a broad metal breech plate, has proven very useful when used judiciously. When obstetrical chains are fastened to the fetus and to the hoist or jack, traction is applied and the fetus is gradually withdrawn. This instrument has great advantages over the block and tackle and wire stretchers used previously, because it allows traction to be regulated and applied upwards, downwards, or to either side. The older block-and-tackle method of traction allowed traction to be applied in only one direction and was much less professional than the fetal extractor. This device must be used with judgement and caution and with epidural anesthesia to control pain because of the great pressures it can produce on the fetus and dam. If the fetus is alive and breathing it should be used intermittently with periods of rest to prevent asphyxia from excessive tension on the respiratory muscles.

Forceps and snares of a wide variety are used to relieve dystocia in ewes and sows, bitches and queens. Knowles' cervical forceps are very satisfactory in swine as are certain wire forceps or snares. These same snares work well in many dystocias in ewes. Snares made of thin twisted wire with a long thin handle are valuable in securing the lower jaw, the limbs or the head and neck since they tighten securely and are much less apt than are chains to slip off and injure the teeth or hooves. The author has found that in an emergency clean hemp twine used for baling hay may be used after disinfection as a snare for the lower jaw or limbs. If a large knot is tied in the cord outside the vulva an obstetrical handle may be used for traction. In dogs "clam shell" forceps, sponge forceps, Roberts' snare forceps, or Hobday's type of forceps are useful.³ The clam-shell type of forcep in which there is a small offset in the handles so that the hinge does not fit tightly and cannot pinch the mucous membrane was preferred.¹⁰ Forceps or snare delivery in multipara is necessarily limited to those fetuses that are in

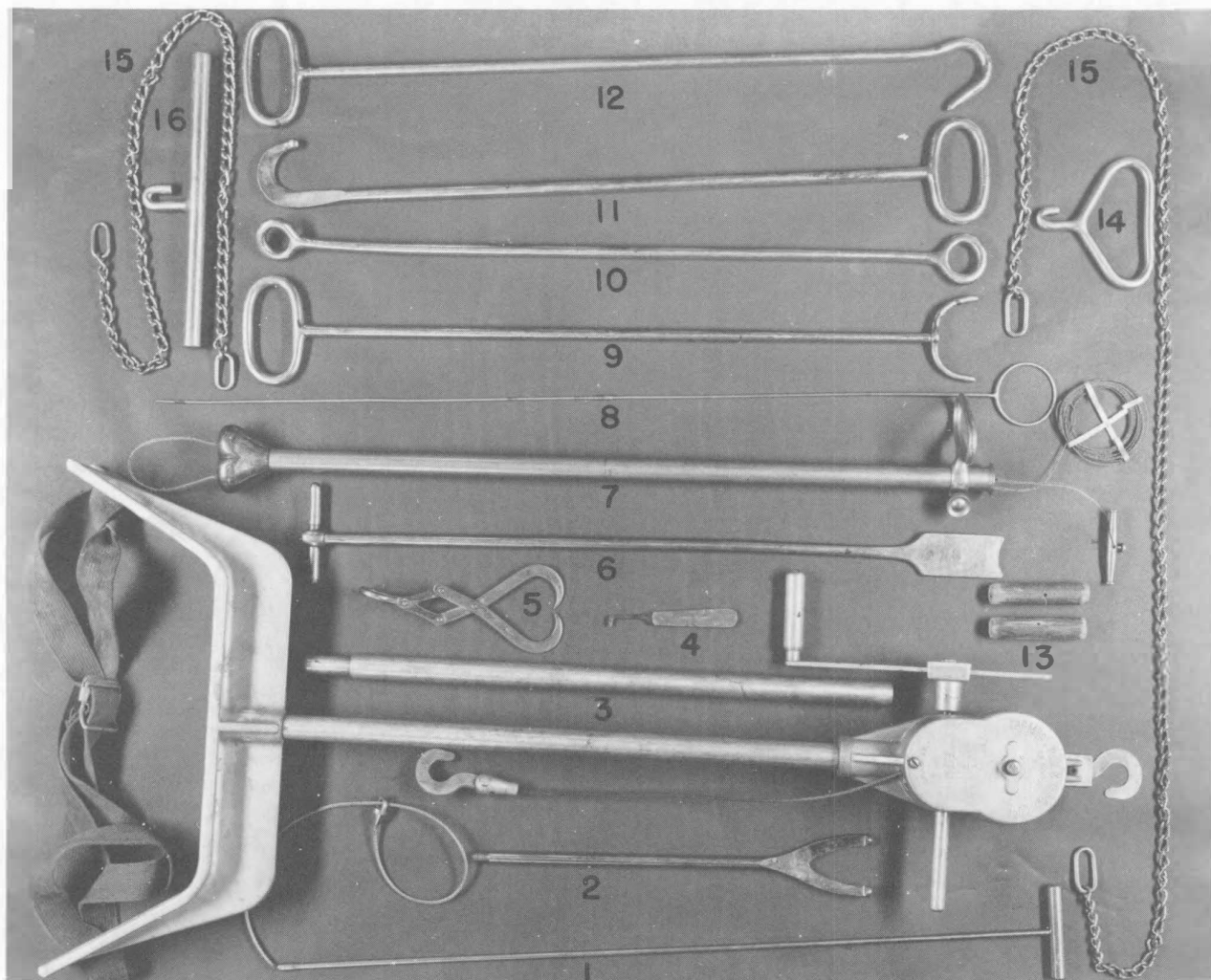


Figure 87. Bovine and Equine Obstetrical Instruments 1. Head snare, 2. Guard's chisel, 3. Fetal extractor, 4. Hoeblade castrating knife, 5. Krey's hook or tongs, 6. Williams' chisel, 7. Fetatome, 8. Threader for fetatome wire, 9. Crutch repeller, 10. Detorsion rod, 11. Williams' bluntpointed cutting hook, 12. Williams' long blunt hook, 13. Handles for wire saw, 14. Muir's chain handle, 15. Moore's obstetrical chains, 16. Gibbons' chain handle.

the pelvic canal or the body of the uterus just cranial to the pelvic inlet. Great care must be used in applying rigid metal forceps or snares to the extremities of living fetuses as lacerations or injuries to the fetus or birth canal are easily produced.

Instruments for section are used in fetotomy to reduce the size of the fetus. These instruments should be kept sharp and in good operating condition. The number and type of instruments are many and each veterinarian usually develops his preferences. Williams stated that there is no place in surgery in which familiarity with an instrument is more important to the operator than in fetotomy.

Knives—A heavy scalpel and a Bard Parker knife are useful in removing a portion of the fetus that may be outside of the body of the cow, as for example, in the operation of decapitation. The hoe or hook-bladed castrating knife is useful within the uterus, particularly the former as it does not cut so deeply into the fetus and is therefore easier to use. These castrating knives are easy to guard with the hand while in the uterus.

Williams' long cutting hook with a blunt point is very useful for cutting ribs.

Long cutting chisels are of three types: Williams, with a slightly concave flat blade; Guard's, with a V-shaped head; and the Ames chisel, resembling a nasal septum

chisel. The usefulness of chisels is limited.

Fetatomes of many types, especially in Europe, are used to protect and guide the fetatome wire.^{1,3,5,12} The two most widely used in America are the Benesch Universal and the Utrecht fetatomes. Fetatomes have the advantage over most chain saws or wire saws in that they can cut at different angles and not just in one caudal direction. The fetatomes use a stiff wire threader or guide to place the wire through the fetatome. There are several types of handles for the fetatome wire. The best type is the one in which the fetatome wire is placed between two interlocking rows of "teeth" that firmly secure the crimped wire when the handles are closed. Large forceps are also satisfactory. Several types of heavy metal rings or an obstetrical chain can be used as a guide or leader to carry the fetatome wire around the fetus. The wire should be of the best grade obtainable; it should be kept clean and free from rust, and after having been used for one fetotomy operation should not be used again. Kinking of the wire should be avoided.

In applying and using the fetatome, the fetatome wire should be securely fastened to the guide or an obstetrical chain unless a loop of wire is used. The guide or chain should always be introduced over the top of the fetus, or dorsally and then downwards or ventrally to take advantage of gravity to help carry the weighted guide around the part of the fetus to be removed. If a chain is used a large handful should be coiled in the hand and introduced as far around or over the fetal part as possible before being released. Otherwise the chain may follow the operator's hand and arm as it is pulled back, thus making it impossible to reach when the hand is passed under the fetal structure to pick it up and complete this phase of the operation. This procedure should always be done against the fetal hair, so that fetal membranes will not interfere with nor complicate the prompt placing of the wire. Occasionally the guide or chain will drop into the nongravid horn, making recovery of it impossible when the hand is passed under the fetus or fetal part. If the fetatome wire is already threaded in the fetatome and a loop of this wire is to be slid up and over an extremity, the head of the fetatome should precede and help guide the loop of wire into place. In sectioning the fetus with a fetatome, the head of the fetatome should be held tightly against the fetus, and the handle of the fetatome held or braced with the other hand and arm placed across the chest or hip as the sawing proceeds.

The newer Utrecht or similar models of fetatomes have a chain fixation plate or hooks behind the handle for attaching obstetrical chains fastened under tension to the fetus. The older Benesch universal fetatome can be modified by welding a chain fixation plate or hooks for at-

tachment of chains to the handle. With these fetatomes the head of the fetatome is located in its desired position and the wire is placed properly and tightened. Before cutting with the wire the head of the fetatome is held in place on the fetus by obstetrical chains, and Krey's tongs if needed, attached to the fetatome handle under tension. This innovation greatly facilitates accurate positioning of head of the fetatome and reduces the expenditure of effort by the operator.

The operator performing the sawing should maintain a constant strong tension on the wire with both arms, and use long, smooth strokes. If bone is encountered the wire will become hot and may break; therefore the position of the wire cutting through bone should be changed frequently, or sawing should be intermittent in order to allow the wire to cool. Breaking of the wire occurs most often on angular cuts. Care should be used in placing the fetatome, to see that the wires are not crossed between the fetatome and the fetus, as this generally results in immediate breaking of the wire. The fetatome wire should be kept taut at all times to prevent coiling, kinking and breaking. If the progress of the sawing is to be investigated, the assistant who is manipulating the wire should be warned so that the operator's hand or fingers will not be cut.

Wire Saws—There are several wire saws that cost less than the fetatome but they usually cut only in one direction, that is caudally. The pipe or guard used to protect the birth passage from the fetatome wire has no specifically designed head or end of hardened steel. Many other types of wire saws protected by metal spiral tubes or tubular pipes have been designed in Europe. The spiral types may be used to cut in more than one direction.^{3,12}

Other more elaborate instruments for section have been devised and used in Europe.³ The widespread acceptance of the fetatome has made for infrequent use of the earlier long blunt-pointed cutting hooks, chisels, and wire saws.

Instruments for Repulsion and Rotation—In repelling the fetus from the pelvic cavity, examining the fetus, or making room for manipulation of the fetus or its extremities, epidural anesthesia and the operator's arm are most commonly used.

Williams' crutch repeller, with or without the removable spike, is very useful when the fetus is firmly impacted in the pelvic inlet. It allows the operator's assistants to provide the strength to repel the fetus, and thus conserves the operator's strength. By use of this crutch the fetus can be repelled downward and forward, upward and forward, or laterally and forward. Kuhn's crutch is strongly advocated³ for the relief of dystocia but it has not become popular in America. Most of the

operations performed by these repelling instruments can be performed with greater facility by the operator's hand and arm.

The fetal rotators or uterine detorsion rods are of a number of types and are used to rotate the fetus when it is in longitudinal presentation in an abnormal position. This abnormal position may be due to a mild to moderate, 90° to 240°, torsion of the uterus. As in repulsion the operator's arms or proper direction of traction on the obstetrical chains will correct many torsions of the uterus or dorso-sacral or dorso-pubic positions of the fetus in large uniparous animals. The so-called Cornell detorsion rod is simple and requires only a 60-inch obstetrical chain and handle to make it complete. Other metal rotators, such as Erikson's, resembling a long-handled twitch with snares and chains to fasten the leg to the handle of the instrument have been used to advantage. In Europe Cammerer's torsion fork is popular and requires two canvas sleeves.³

It is highly desirable that all long-handled instruments, such as the long blunt hook, the blunt-pointed cutting hook, and chisels be solid and rigid, as they often have to be twisted within the uterus. If they are jointed the instrument can be twisted or rotated in only one direction.

In difficult or prolonged dystocia proper **lubricants** for the genital tract are essential. When the mucous membrane of the vulva and vagina is dry, mild, non-irritating soap, such as Ivory soap flakes, and water or bland liquid soap may suffice in cases needing slight lubrication. In cases requiring much lubrication epidural anesthesia is necessary to prevent the animal straining and throwing out the lubricant, and to cause sufficient relaxation so that the lubricant can flow about and cover the fetus and uterine, cervical, vaginal and vulvar walls. Mineral oil, 1 or 2 quarts, is only fairly satisfactory. Older practitioners used linseed infusions or lard or more recently canned cooking-fat preparations like "Crisco." A blended mixture of white vaseline and 10 percent boric acid has been recommended especially for fetotomy operations.⁵ To remove this tenacious greasy lubricant from the arms and hands a good detergent or mechanic's soap is recommended. The newer commercial lubricants such as **Lubrivet** and other lubricating jellies in tubes or jars or carboxymethylcellulose solutions^{39a} are good. These solutions or lubricants may be rubbed on the fetus and walls of the birth canal after being pumped in with a stomach pump and tube. In smaller animals the rear parts may be elevated so that the lubricant runs in by gravity. In severe, prolonged operations the lubricant may have to be applied 2 or more times or as frequently as the fetus or birth canal becomes dry. In rotation of the fetus

on its long axis lubricants are essential. They help to protect the mucous membranes from irritation, infection, trauma, and even rupture, besides making obstetrical manipulations and operations easier in the prolonged "dry" cases of dystocia associated with a dead or emphysematous fetus.

Other equipment for obstetrical operations should consist of two clean enamel, stainless steel or plastic pails, soap, several types of antiseptics, common surgical instruments including syringes, needles, scalpels, scissors, forceps, suture needles, and various types of sutures, sterile drapes and towels, sponges, razor, cotton, oxytocin, anesthetics for local and epidural anesthesia, tranquilizers and general anesthetics.

Epidural Anesthesia or Analgesia

Epidural anesthesia in the cow and mare is one of the most useful tools for aiding the operator and relieving pain in the patient suffering from severe dystocia. Prior to this useful tool straining was combatted by a noselead, twitch, sharp object pressed down on the back and even tracheotomy. The former pain-producing techniques are very imperfect or only shortlived. The technique of epidural anesthesia was introduced into the United States by Benesch in 1926.² In obstetrical work epidural anesthesia is used frequently because it stops abdominal straining and makes mutation of the fetal extremities, repulsion of the fetus, correction of breech presentation and uterine torsion much easier. It abolishes or reduces all pain and is therefore more humane and should be administered when great power is used as in some forced extractions. It greatly increases the speed, ease, and safety to the operator and patient in fetotomy operations. With proper epidural anesthesia the animal stands quietly without moving about or lying down, which is helpful to the operator. Often the cow that is down and refuses to stand will rise and stand normally following the administration of epidural anesthesia. Defecation is suspended. The animal does not rapidly expel lubricants pumped into the uterus. When used in cesarean section it controls straining and prevents intestinal prolapse through the operative incision. It is used to aid replacement of prolapse of the vagina, cervix, uterus, rectum, or bladder. By controlling straining, it may prevent prolapse of the uterus immediately after a difficult parturition. It alleviates symptoms of straining caused by severe vulvitis or vestibulitis. The use of epidural anesthesia is nearly free of danger and is seldom if ever contraindicated. Normal involution of the uterus is not interfered with and epidural anesthesia does not cause or fa-

vor retained placenta. Epidural anesthesia is not required in every dystocia case. In those cases in which a rapid and normal course of parturition is expected or a simple easy manipulation can correct the dystocia, it need not be used.

The technique for administering epidural anesthesia, particularly in the cow, is simple and easily mastered. Most veterinarians use a 16- or 18-gauge 1-1/4" to 2" needle. The site for insertion of the needle is determined by elevating and lowering the tail and feeling where the vertebral joints are located by the depression and movement between the vertebrae. The joint between the first and second coccygeal vertebrae is the most moveable in the cow. In palpating caudally from the sacrum, the first vertebrae joint in which movement can usually be felt is between the last sacral and first coccygeal vertebrae. After properly shaving and disinfecting this site, the needle is inserted in the cow between the first and second coccygeal vertebrae or the first coccygeal and last sacral vertebrae. The author prefers the latter site in the cow. The needle is introduced at a 10 degree angle caudally from the perpendicular, and strikes the bottom of the vertebral canal of the last sacral vertebra. This readily determines the depth at which the anesthesia should be injected. Between the first and second coccygeal vertebrae the needle may go entirely through the spinal nerves and joint. Inserting the needle in the mare is more difficult. It is introduced at a slightly greater angle caudally, 30 degrees from the perpendicular, than in the cow, about one inch cranially to the long coarse tail hairs. The veterinarian should be careful to insert the needle directly on the midline. In the cow the needle is inserted about 3/4 to 1-1/2 inches deep, depending on the size, amount of fat and the thickness of the tail. In the mare the needle is usually inserted 1-1/2 to 2-1/2 inches deep. If the needle is inserted carefully one can often feel the point of the needle "pop" through the thick connective tissue sheath covering the nerve. When the needle point has reached the proper location the anesthetic solution flows easily out of the syringe into the epidural space. If the needle is not at the proper site the solution is injected with difficulty. If the anesthetic does not contact the nerve the tail does not become flaccid, and anesthesia of the perineum is not produced. If anesthesia of the motor nerves of the tail is not evident within 3 minutes, the anesthetic was not injected properly. Occasionally the needle strikes the artery or vein ventral to the nerve, and blood will flow from the needle. This should be of no concern except that it indicates the needle is at the proper site for injection, or just below the nerve. It should be noted that this epidural injection is a nerve block and not a spinal anesthesia. The injection is out-

side the dura mater caudal to the end of the spinal cord. The spinal cord, containing the spinal fluid, terminates between the second to fourth sacral vertebrae in the cow and the first to third sacral vertebrae in the mare.¹

The amount of anesthetic solution to be injected varies with the type of solution, the weight or size of the animal, the species of animal, and the degree of anesthesia desired. In most obstetrical cases the solution should be injected in repeated small injections, so that the animal remains standing. If too much is given the animal will stagger, and possibly fall and injure itself. The author prefers to use a 2 percent lidocaine or procaine solution in 5 to 10 ml. amounts for 600-pound to 1300-pound cows and mares. Lidocaine produces a more rapid and deeper sensory anesthesia than procaine. If 1 percent procaine solution is used the amount of solution injected should be nearly doubled. This anesthesia will last about 1-1/2 to 2 hours. This time may be nearly doubled by adding 0.5 to 1 ml. of a 1:1000 solution of epinephrine. Two percent procaine penicillin in 5 to 8 ml. amounts produces satisfactory epidural anesthesia. When the animal is recumbent and the operator desires it to remain so, the animal should be placed on its sternum and as much as 20 to 50 ml. of 2 percent procaine or its equivalent may be injected epidurally without any adverse effects and with good sensory and motor anesthesia of the rear quarters. The larger amounts of anesthetic solution are forced cranially to anesthetize the motor nerves to the rear limbs.

Products containing benzyl alcohol, propylene and polyethylene glycol when injected into the epidural space produce a prolonged anesthetic effect lasting for 4 to 40 days or more by destroying the nerve fibers. In dairy cattle or horses this is very undesirable; as the animal's rear parts and tail become covered with fecal material because the tail cannot be elevated at the time of defecation and micturition. In rare instances when prolonged destruction of the nerve is desired, 5 to 10 ml. of 70 percent grain alcohol may be injected epidurally. In these instances recovery may be delayed 6 months or more. During the summer months flies and maggots may become a problem if the perineal region is not cleaned regularly.

Epidural anesthesia in sheep and goats is practical but seldom used as the abdominal contractions are not strong enough to interfere greatly with manual manipulations of the fetus. Using an 18-gauge needle 1 to 1-1/2 inches long, the operator may inject 2 to 4 ml. of a local anesthetic solution between the last sacral and first coccygeal vertebrae or between the last two sacral vertebrae.

Epidural anesthesia is seldom used in multipara except

for cesarean section because of the number of fetuses and the long period of parturition together with the resulting interruption of labor which would require a prolonged period of observation and assistance for each fetus as it entered the pelvic cavity. Epidural anesthesia or analgesia is obtained in dogs and swine by entering the lumbosacral space with a short-beveled, 2 to 5 inch, 18 to 20 gauge, spinal needle with stylet. The space is located on the midline a short distance caudal to a line at right angles to the spinal column and at the level of the crests of the dorso-iliac spines.^{7,8,9} After proper shaving and disinfection of the site, local subcutaneous anesthesia may be administered with a small needle. The spinal needle is passed perpendicularly into the lumbosacral space. When it penetrates the ligamentum flavum or the interarticular spinous ligament a distinct "pop" is felt as the point of the needle enters the epidural space. The stylet should be removed and aspiration applied on the needle to be sure the needle did not penetrate a blood vessel or the subarachnoid space containing the cerebral spinal fluid. This is unlikely as this space is small or not present at this level and is difficult to enter in bitches and sows. The dose of 2 percent lidocaine for epidural anesthesia in the dog is 1 ml per 7.5 to 10 pounds of body weight and for swine is 1 ml per 20 pounds of body weight. If 4 percent procaine is used in swine the dose is 1 ml per 10 pounds of body weight. In dogs 2 percent procaine at a rate of 1 ml per 5 pounds of body weight is recommended.^{7,8,9}

In recent years European veterinarians have reported on the extensive use of sympathomimetic agents and blockers of parasympathomimetic receptors resulting in a tocolytic effect and relaxation of uterine muscle in a variety of obstetrical cases in all species of animals. These have included dystocias due to abnormal postures and positions of the fetus, uterine torsion, fetotomies and cesarean sections. The advantages in using these agents, clenbuterol (**Planipart**) or isoxsuprine (**Hanigif**) are especially indicated in prolonged dystocias with dead fetuses. The nonsurgical management of dystocia was greatly facilitated with no increase in calf mortality retained placentas or adverse effect on postpartum uterine involution. These tocolytic agents act rapidly after injection with muscle relaxation lasting for several hours.^{1a,8b} It is hoped that these tocolytic agents will soon be available to veterinarians in the U.S.

Other Forms of Obstetrical Anesthesia

General anesthesia is often indicated in the mare with severe dystocia when extensive mutation, fetotomy pro-

cedures, rolling of the mare to relieve torsion of the uterus or a cesarean operation must be undertaken. General anesthesia is often begun by administering a tranquilizer, such as **Rompun**, followed by a short-acting intravenous anesthesia such as 5 to 10 percent dextrose solution to which thiamyl sodium or thiopental sodium have been added or ketamine HCL. After anesthesia has been induced additional amounts of the former may be given intravenously to maintain anesthesia.¹³ These products have largely replaced the older chloral hydrate and pentobarbital intravenous solutions for equine anesthesia. In the more modern equine clinics inhalation anesthesia of halothane may be used since this product is safe and relatively nontoxic even when given over a prolonged period of time. If the fetus is alive and saving it is desirable, tranquilizers, epidural or local anesthesia should be used. On occasion the intravenous or inhalant anesthetics may be used when the fetus is alive, even though the anesthetics cross the placenta, if the fetus is removed immediately after these anesthetics are administered. If the mare is to be given general anesthesia this should be done in a location large enough to work in with ease. With the mare anesthetized, its feet should extend away from the body in a normal manner so that no pressure is placed on the abdominal cavity. The mare may be rolled from one side to the other, to help the operator. For example, if the head and neck of the fetus is retained along the right side of the fetus in anterior presentation the mare should be laid on her right side so the head and neck of the fetus are located above and not beneath its body, where the weight of the fetus would make correction of the deviated head and neck difficult or impossible. Assistants may apply backward pressure to the fetal head through the relaxed upper flank of the mare.

For cesarean section in the cow, tranquilization, epidural, paravertebral, or local anesthesia or combinations of these may be used. When rolling to correct torsion of the uterus in the cow, 1.5 to 2 ounces of chloral hydrate may be given orally in capsules or by stomach tube, or 0.5 to 1 ounce given intravenously to narcotize the animal is still useful.

For cesarean section in the sow, a tranquilizer followed by local anesthesia of the operative site may be used.^{12b} Spinal anesthesia has been administered to sows and bitches by injection of procaine or lidocaine into the epidural space of the spinal cord at the lumbo-sacral articulation.^{7,8,9} Presently atropine is given as a premedication followed by an ultra-short acting barbiturate and a light plane of halothane or methoxylflurane anesthesia. **Innovar**, a neuroleptanalgesic, has also been used and followed by **naloxone** after the cesarean operation to reverse its action in the bitch and pups. Local anesthesia

may be used in the bitch in either of the above procedures to reduce exposure to the anesthetic. **Doxapram**, a respiratory stimulant, may aid recovery of pups or foals with a small amount given under the tongue or parenterally.¹³ In the bitch and cat an ether, morphine and atropine combination was formerly used as a general anesthetic during cesarean operations. In general the long-acting barbituates are not desirable because of their depressing effect on live fetuses.

The proper use of tranquilizers and local and general anesthetics in dystocia and other obstetrical operations is frequently necessary and results in easier, safer, and more rapid handling of birth-related problems, to the great benefit of both the animal and the operator.

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Chapter IX

OBSTETRICAL OPERATIONS

In handling dystocia there are numerous operations or procedures that the veterinarian should be able to perform or use. Following a careful examination, the most conservative procedures should generally be undertaken in the interest of the owner, the veterinarian, the animal, and the fetus. The principal purpose of obstetrical operations is to deliver a viable fetus and to prevent injury to the dam. After a careful assessment of each obstetrical case the procedure selected should best achieve this purpose. Radical and heroic handling of dystocia is seldom necessary and then only when more conservative treatments have failed or when examination indicates the condition is such that ordinary routine methods or a combination of them will not effect relief. In most cases of dystocia one or more combinations of the major obstetrical operations are performed. The plan of operation should be carefully made with alternatives in case one procedure is not successful. If assistance or consultation is needed it should be obtained as soon as possible. In performing obstetrical operations on large animals it is necessary for the veterinarian to conserve his strength by working with both arms and by using lay assistance whenever possible. If the fetal membranes interfere with the obstetrical operations the offending portions of the membranes should be removed manually. The obstetrical operations may be divided into four major classifications: mutation, forced extraction, fetotomy and cesarean section. Laparohysterectomy is only performed in occasional instances in the bitch or queen. For excellent illustrations of various mutation and fetotomy techniques the student is referred to the following reviews.^{2-9,39a}

Sloss⁴² reported the incidence of bovine dystocia on 1600 properties involving 126,790 Australian dairy and beef cows as recorded by 13 country veterinary practices and the results of different methods of handling the 2480 dystocias. Mutation and forced extraction were most commonly employed in dairy cattle and comprised 77.8 percent of the cases of dystocia. While fetotomy and cesarean section were more commonly used in beef cattle and comprised 16.6 percent and 4.7 percent, respectively, of the total number of dystocias. These figures were nearly similar to those cited by other authors. The maternal death rate was 6 percent with a rate of 3.1 per-

cent in operations involving mutation and traction, 16.6 percent after fetotomy and 17.9 percent after cesarean section. Thirty two percent of the dystocias in dairy cattle were in heifers while 70.6 percent in beef cattle were in heifers.

Mutation

Mutation is defined as those operations by which a fetus is returned to a normal presentation, position, and posture by repulsion, rotation, version, and adjustment or extension of the extremities. Normal birth will proceed in uniparous animals only with the fetus in anterior or posterior longitudinal presentation, dorso-sacral position, with the head, neck and limbs extended. Most multipara can have a normal birth with the fetal limbs folded alongside of or beneath the body, since the limbs are small and flexible. In multipara, fetuses may be in a dorso-ilial or dorso-pubic position and be born without difficulty. In unipara only premature or very small fetuses may pass through the pelvis in dorso-ilial or dorso-pubic position or with a flexed limb or limbs. In ewes, the fetus may often be born without assistance in anterior presentation with one forelimb retained beneath the body. After the veterinarian has brought each part of the fetus into its normal posture, the cause of dystocia is usually relieved and the fetus will be expelled normally, or parturition aided or completed by traction.

Repulsion, sometimes called retropulsion, consists of pushing the fetus out of the maternal pelvis or birth canal into the abdominal cavity and uterus, where space is available for the correction of the position or posture of the fetus and its extremities. In nearly all cases in which expulsion is used, epidural anesthesia is indicated since repulsion frequently produces violent straining on the part of the animal. When repulsion is used, the portion of the fetus engaged in the pelvis is pushed cranially. Because the fetus and uterus are in the form of an arc in the cow, the opposite end of the fetus may be pushed somewhat nearer the pelvis. Repulsion is usually necessary because the birth canal or pelvic cavity is so narrow and so confining that it is impossible to correct deviations in po-

sition or posture without providing more room in which to manipulate the fetus or its long extremities. Besides its common use for repelling a portion of the fetus out of the pelvis, repulsion may also be used to force a portion of the fetus—usually the proximal portion of an extremity and the part of the body to which it is attached—cranially, dorsally, ventrally, or laterally in the uterine and abdominal cavity so that sufficient room is provided to extend the flexed extremity with facility.

Repulsion may be accomplished by the operator's arm, the arm of an assistant, or by a crutch repeller. If the latter instrument is used it should be guarded by having the operator's hand on the crutch part of the repeller as force is applied, so that slipping of the crutch and possible uterine laceration or rupture is avoided. In anterior presentation the crutch or hand of the operator is usually placed on the fetus between the shoulder and chest or across the chest beneath the neck. In posterior presentation it is placed in the perineal region over the ischial arch. Epidural anesthesia is of great value especially in large animals, because the fetus after being repelled is not immediately forced back into the pelvis by straining, and therefore it is easier for the operator to correct the abnormal posture or position. If the crutch repeller is used and left in place the person applying the outside force should be properly braced and balanced so if the crutch slips or becomes displaced it will not be forced cranially, possibly through the uterine wall. If it slips it should immediately be withdrawn or replaced. It is somewhat safer to use an assistant and under the operator's direction have him repel the fetus with one arm while the operator's arm corrects the abnormal posture. The only disadvantage to this method is that in heifers with a small birth canal, room for two arms is restricted. In ewes, does, and sows, repulsion is performed by the arm and hand, or by the finger in bitches and queens.

Having the animal standing or with its rear parts elevated if it is recumbent, is essential to make room available for repulsion. Repulsion is difficult or impossible in the recumbent animal resting on its sternum, as the abdominal viscera are forcing the fetus back toward the pelvis. If the animal is recumbent it should be laid on its side with its four legs extended. In ruminants the dam should be resting on the left side so the weight of the rumen does not press on the fetus and uterus. Excessive repulsion may be dangerous, especially in cases in which dystocia has existed for some time, because the uterine wall is often tightly contracted around the fetus. The uterine cavity thus nearly ceases to exist, and hence rupture of the uterus is liable to occur. In other countries uterine relaxants and spasmolytic drugs have been advocated and used.² These have not been available for use

in the U.S. In cases of neglected dystocia or of emphysema of the fetus, the repulsive force should be carefully controlled. Frequently satisfactory repulsion is impossible and this is the reason why the handling of prolonged dystocia cases is difficult and the prognosis is guarded to poor. In large animals, early diagnosis of minor abnormalities causing dystocia may preclude the need for epidural anesthesia and with the animal standing the fetus can be repelled and its posture or position corrected between abdominal contractions.

Rotation is the turning of the fetus on its long axis to bring the fetus into a dorso-sacral position. This position is necessary in all but very small fetuses in uniparous animals and is the usual presenting position even in multiparous animals. In the latter species an abnormal position of the fetus seldom causes dystocia due to the small size of the fetus compared with the size of the pelvic cavity or inlet. In the cow the presence of the fetus in a dorso-ilial or dorso-pubic position frequently is accompanied by a 90- to 180-degree torsion of the uterus.⁵⁶ In 90-degree torsion of the uterus twisting of the birth canal is often not noticeable. It seems very unlikely that an 180-degree torsion with its accompanying marked twisting of the birth canal would go unnoticed by an experienced veterinarian. In the dorso-pubic position of the fetus in the cow, a rectal examination and examination of the relation of the broad ligaments and the uterine arteries to the uterus, would reveal whether torsion of the uterus existed and indicate the direction for rotating the fetus in correcting the twisted uterus. **In the mare** and multiparous animals in which the fetus lies in the uterus in a dorso-pubic or dorso-ilial position during pregnancy with the navel cord extending laterally or dorsally toward the uterine attachment of the broad ligament and uterine wall, the fetus must rotate 90 to 180 degrees before entering the pelvic inlet in a dorso-sacral position. If rotation is not complete by the second stage of parturition, dystocia may result. In multiparous animals with the fetus in a dorso-pubic position the nose of the fetus may catch on the pelvic brim in anterior presentation, or the buttocks may catch on the brim of the pelvis in posterior presentation. These positions and postures are common causes for dystocia in dogs.²⁵

To relieve dystocia in unipara by rotation of the body of the fetus, it should be repelled cranially out of the pelvic cavity. If this cannot be done, due to the contracting uterus, it indicates that the dystocia has existed long enough to also result in a dry mucous membrane of the birth canal. In this case much careful lubrication of the birth canal and fetus is necessary to make rotation of the fetus within the confining structures possible and easier without injuring the uterine or vaginal walls. In

dorso-iliac positions repulsion is often not necessary but may be helpful. Lubrication of the fetus and birth canal, caudal and downward traction on the extremities, and rotation of the fetus with the operator's arm in the birth canal, readily corrects this mild abnormal position. After the body of the fetus in anterior presentation, dorso-pubic position, is repelled out of the pelvis, leaving the fetal limbs in the pelvic cavity, chains are fastened to the fetlocks and cross-traction is applied by two assistants. Depending upon which way the fetus is to be rotated one leg is initially pulled upwards, then horizontally to the left or right and then downwards while the other leg is being pulled underneath the first leg downward and obliquely to the right or left. This type of traction causes a rotation of the body of the fetus that is aided by the operator placing his arm and hand under the withers or body of the fetus and elevating it to the level of the pelvic brim, using the pelvis as a fulcrum, and then pushing the fetus obliquely to either the left or right.

To prevent the hip-lock condition in anterior or posterior presentation Ball^{3,39a} recommended rotation of the fetus so that the fetal hips engaged the maternal pelvis in an oblique manner to take advantage of the widest pelvic diameter. (See Figure 1.) This could be accomplished by applying moderate traction to the fetus and inserting the arm between the fetal legs, and over the neck in anterior, and between the rear legs in posterior presentation, and rotating the fetal body and pelvis the desired angle. The fetus is withdrawn by caudal and lateral traction, first one hip and then the other, through the pelvic girdle of the dam.

In occasional prolonged cases of dystocia in anterior presentation, the head and neck may be an obstacle to rotation and have to be amputated before rotation can be accomplished. In posterior presentation the fetus is rotated in a like manner, with the operator's hand and arm under the buttocks. This method of cross-traction is superior to placing traction directly backward on one limb and twisting the opposite limb around the fulcrum thus established. This latter technique causes the fetus to become impacted in the maternal pelvis and thus resist rotation, and a great strain is placed on the joints and ligaments of the leg that is twisted around the one to which traction is being applied. In the former techniques impaction of the fetus in the pelvis is reduced to a minimum, and elevating the body of the fetus makes correction of the abnormal position rapid and easy. If correction of the position is difficult in one direction, torsion may be present, and the direction of traction may be increasing the degree of torsion. If this is the case, the fetus should be rotated in the opposite direction. In mild cases diagnosed early in parturition or where the fetus is small,

the fetlock protruding from the vulva may be flexed and used as a means of exerting a moderate twisting action on the leg to assist rotating the fetus.

In a few cases, rotation may require the use of the detorsion rod or Cammerer's fork as described under torsion of the uterus. In these cases the rod is fastened to the two limbs after lubrication of the fetus and the birth canal and by repulsion and rotation the position is corrected. In ewes and sows the hand and in bitches and queens the finger applied to or alongside the chest or buttocks after lubrication will usually repel and then rotate the fetus into a normal dorso-sacral position. In these smaller animals forceps may also be used with care to rotate the fetus.

Version is the rotation of the fetus on its transverse axis into an anterior or posterior presentation. This is done most often in the mare in transverse ventral presentation and in rare cases in the cow, ewe, doe and bitch in transverse presentation. Transverse presentation in the mare occurred about 1 in 1000 pregnancies.⁴⁴ Version is usually limited to 90°. By repulsion on the cranial or caudal end of the fetus and traction on the other end, the transverse presentation is changed to a longitudinal presentation. If possible the fetus should be turned into a posterior longitudinal presentation, as that prevents the head and neck from complicating the correction of the abnormal presentation or posture. In the mare partial fetotomy is often indicated before version is attempted in transverse ventral presentation. Often version is only through a relatively small arc if the fetus is lying obliquely rather than in a true transverse presentation. In the tubular type of uteri in domestic animals, version through a 180° arc such as from posterior to anterior presentation is rarely possible and should not be attempted.

Extension and Adjustment of the Extremities is the correction of abnormal postures usually due to flexion of one or more of the extremities causing dystocia. Flexion of the head and neck causes dystocia in all species. Flexion of the limbs usually results in dystocia in uniparous animals but only rarely in multiparous animals. Corrective procedures are difficult and often impossible within the confines of the pelvic cavity. The fetus must usually be repelled out of the pelvis into the larger uterine and abdominal cavities to have sufficient room for the correction of abnormal postures. This is particularly true in the large uniparous animals, in which the fetal extremities are long. Many of these abnormal postures may be caused by the distal portion of the fetal extremity being caught on the pelvic brim, and are aggravated when the body of the fetus passes over this extremity, thereby resulting in greater flexion of the extremity and even its extension beneath the body. The act of repulsion of the fetus cranially into the uterine and abdominal cavities

tends to correct the deviated extremity or abnormal posture. Three basic mechanical principles are necessary to effect a prompt, easy correction of a flexed extremity (see Figure 88).

(1) **Repulsion of the Proximal Portion of the Extremity** such as the shoulder or chest is performed in anterior presentation in the correction of a flexed fetlock, carpus, elbow, or shoulder joints with the forelimb extended beneath the body; or the head and neck flexed alongside, beneath or over the body of the fetus. In posterior presentation repulsion is performed on the buttocks, stifle, or tarsus when the hind limbs are flexed at the stifle, tarsus, fetlock, or hip. In the latter condition the legs extend beneath the fetus, a breech presentation.

(2) **Lateral Rotation of the Middle Portion of the Extremity, Carpus, Tarsus, or Neck**—Lateral rotation and repulsion of the flexed tarsus, carpus or neck into the cranial and lateral flank region provides adequate room in most cases for the medial extension of the fetlock or nose into the pelvic cavity. In small equine or bovine fetuses, if the operator firmly grasps the metacarpus or metatarsus, he can with the same motion perform both repulsion and lateral rotation as well as extension of the fetlock into the pelvic cavity. In larger fetuses the operator may require a crutch repeller, or even better an assistant's arm, to force the tarsus or carpus laterally and cranially while the operator brings the fetlock medially and caudally into the pelvic cavity. This latter procedure allows the operator to cup or flex the pastern in his hand so that as the limb is extended the hoof of the fetus will not catch, tear, or lacerate the wall of the birth canal as the foot is drawn into the pelvic cavity.

(3) **Traction on the Distal Portion of the Extremity** such as the pastern, the lower jaw or, until these distal structures can be reached, the structures between the body and the distal portions of the extremity, is applied to extend the limbs or head and neck. This traction may be applied by the hands and arm, a chain, Krey's tongs or a snare. When the fetus is in breech presentation with the legs extended beneath the body, the fetus is repelled cranially out of the pelvic cavity and into the right or left flank. The hand and arm is slid down the tibia on the opposite leg and by traction the leg is pulled into a hock-flexed posture and then handled as described. In cases in which the head and neck are deviated alongside the anteriorly presented fetal body the fetus is repelled cranially and laterally into the flank of the cow on the side opposite to the head so that as much space as possible is provided in the other flank to allow correction of the deviated head and neck. By traction with the fingers in the orbits, around the lower jaw, in the angle of the mouth, by a snare around the lower jaw or small hooks in the orbits, the head can usually be pulled lat-

erally back to the pelvic inlet without twisting the neck. The head is then returned to its normal posture by manual traction, elevation or rotation of the head, and lateral repulsion on the neck. During these procedures the muzzle of the fetus should be guarded to make sure the lower incisor teeth do not lacerate the uterus, or the lower jaw catch on the pelvic brim of the dam, especially if the type of traction applied causes the mouth to gape. When the dam is recumbent the deviated fetal head should be located in the upper flank before mutation procedures begin. Otherwise the weight of the fetal body resting on the head and neck would make correction nearly impossible.

The combined use of these three mechanical principles will relieve almost all abnormal postures. In rare cases, in order to obtain more room in which to perform these maneuvers when the uterus is contracted tightly around the fetus, a partial fetotomy may be necessary, such as amputation of a forelimb. In multipara, mutation of the fetus is not generally required except in deviation of the head and neck in anterior presentation, impaction of a large fetus in the pelvis in breech presentation or in dorso-pubic position when the nose or buttocks of the fetus may catch on the pelvic brim of the dam as the fetus enters the pelvis. By using the finger in the vagina and manipulating the canine or feline fetus through the abdominal wall and floor with the opposite hand these abnormal postures may usually be corrected. Occasionally forceps or snares may be indicated. In a few cases dystocia in cattle is observed due to the impingement of the elevated tail on the dorsal border of the pelvic inlet in posterior presentation. Repulsion of the fetus, holding the tail against the perineum and applying traction to the rear limbs corrects the dystocia. Kuhn's crutch was very useful in various mutation operations in the mare and cow.³ Although the theoretical uses of the instrument are many, it has not proved useful in the author's practice.

Mutation of the fetus must be performed carefully, cautiously, and in a gentle manner in all animals. These manipulations can take place only at the level of or just below the pelvic brim. The earlier the dystocia is diagnosed, the easier is mutation of the fetus accomplished; conversely, the longer aid is withheld or delayed, the more difficult or impossible it is for mutation to be successful. This is true, but to a lesser extent, in the other major obstetrical operations.

Forced Extraction

Forced extraction is defined as the withdrawal of the fetus from the dam through the birth canal by means of the application of outside force or traction. Traction should

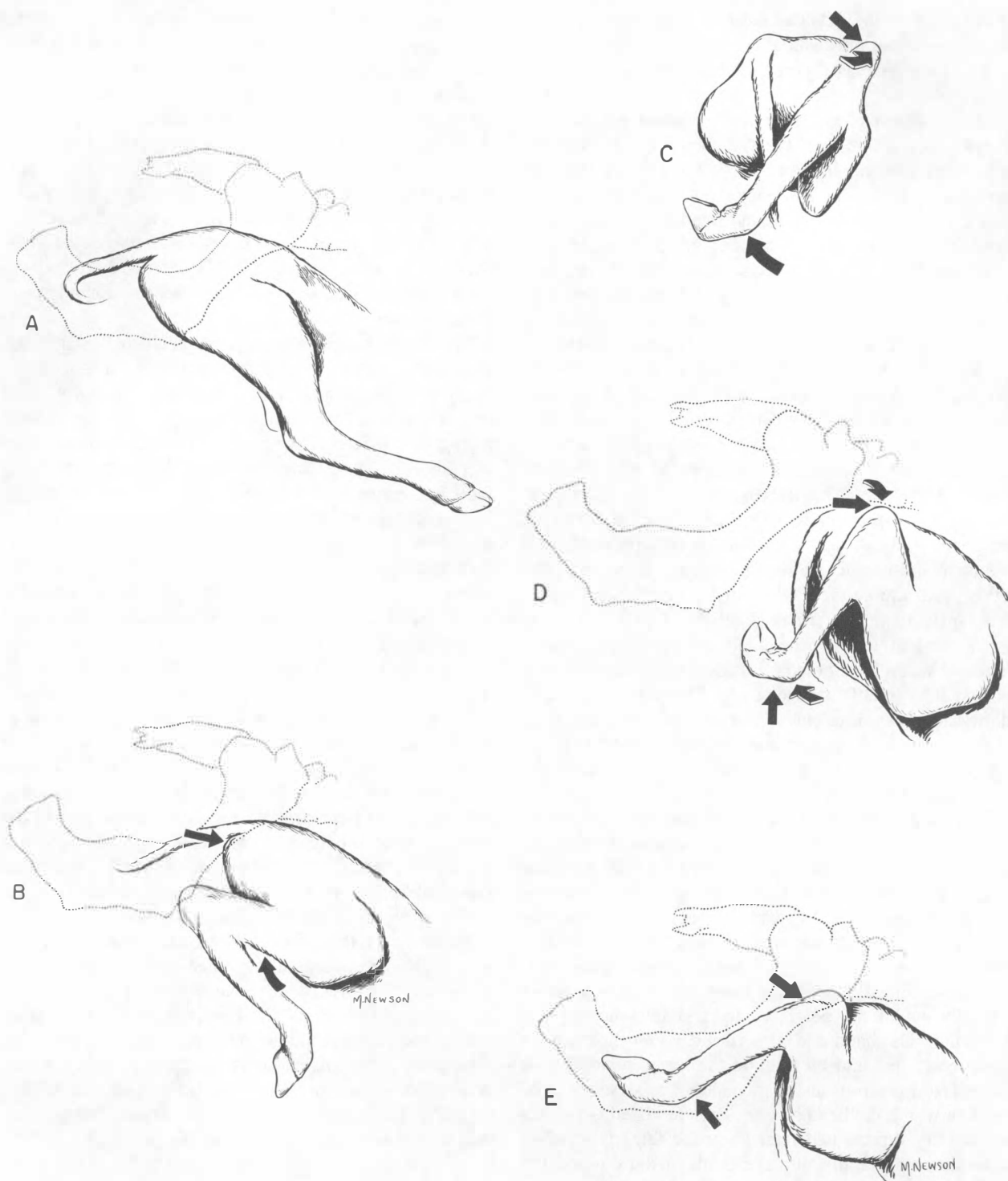


Figure 88. Procedures followed in mutation of deviated fetal extremities: A. Lateral view of a breech presentation of a bovine fetus. B. By repulsion on the buttocks and traction on the tibia the leg is drawn into a hock-flexed posture. C, D and E. caudal and lateral views show how, by upward repulsion and lateral rotation on the hock and medial and caudal traction on the fetlock and pastern, the leg is extended into the pelvis.

be applied only when the abdominal muscles of the dam are contracting and pulling the pubis cranially to provide the greatest pelvic diameters for the passage of the fetus. If traction on the fetus is applied when the abdominal muscles are relaxed the pelvic floor is pulled caudally reducing the size of the pelvic opening.^{3,39a} This intermittent traction may prevent asphyxiation of the fetus if he should be breathing and it is also less stressful for both the fetus and the dam. Since the widest diameter of the bovine fetal pelvis is between the greater trochanters and the widest portion of the maternal bony pelvic inlet is the dorso-pubic, not the bisiliac, diameter (See Figure 1), this information is used to assist withdrawal of a large fetus through the birth canal by rotating the fetus so the greatest diameters of the fetal and maternal pelvis coincide.^{39a}

Manner and Dangers of the Application of Traction Instruments to the Fetus—In anterior presentation obstetrical chains may be applied to the pasterns or above the knee or elbow. If the fetal membranes prevent the prompt application of the chains or snares they should be broken, ripped away, or pushed to one side. The chain should be tightly fastened around the pastern before applying traction or it may slip down over the coronary band of the hoof and when traction is applied the hoof may be pulled off. Applying the chains above the fetlock may be satisfactory in almost all cases but in rare cases excessive traction and tightening of the chain over the epiphysis or "break joint" may fracture the leg. For these reasons many veterinarians place the noose of the obstetrical chain above the fetlock and place a half-hitch around the pastern. This prevents the chain from sliding down over the coronary band and distributes the force over the two sites. Some place the large terminal link in the obstetrical chain ventral to the pastern and pass the chain between the claws of the bovine fetus. This raises and extends the toe and may avoid its catching on the brim of the pelvis.

In anterior presentation a snare may be applied around the lower jaw and tightened firmly so that with traction it will not slip and fracture the dental plate. Obstetrical chains around the lower jaw will not tighten sufficiently, and generally slip off, often damaging the incisor teeth. Excessive traction on the jaw should be avoided, as the jaw bones are not strong and fracture may occur. Moderate traction applied by one man is all that can safely be used on the lower jaw of a bovine fetus. A loop of obstetrical chain around the neck behind the head is used occasionally for traction when the fetus is dead; but the head and muzzle must be directed with the hand so that they will not become deviated. This technique is dangerous to a live fetus as it may cause injury to the spinal

cord and vertebrae in the occipital region. A loop of obstetrical chain is more commonly used around the poll, under the ears and through the mouth in the manner of a "war bridle" for applying traction to the head. This causes the mouth to gape when traction is applied; the operator should therefore watch for this and protect himself and the birth canal from injury by the sharp incisor teeth. Pinching the large link in the end of the obstetrical chain noose in a vise in such a manner that it catches on the chain, thus preventing the chain noose from tightening when traction is applied has been recommended.⁵⁴ A commercial head snare is available that also overcomes gaping of the mouth. By the use of blunt or knobbed Krey's hooks or short obstetrical hooks on a loop or cord in the orbits, traction may be applied to the head.^{3,4} This technique is safe unless excessive traction causes fracture of the facial bones. A technique in which an incision is made in the floor of the mouth anterior to the tongue, extending through the skin between the mandibles has been described. A loop of obstetrical chain is then passed over the lower jaw, behind this incision, and the opposite end of the chain is passed through the incision and tightened.⁵⁶ This provides a firm, solid hold on the lower jaw that will not slip and by means of which a large amount of traction may be applied. It is used most satisfactorily in dead fetuses, but even in live fetuses the wound heals quite rapidly after birth. The long or short blunt hook placed between the rami of the mandibles is not satisfactory because it frequently slips, or with moderate traction may cause a separation of the symphysis of the mandible. In a dead fetus the long blunt hook may be passed through the mouth into the pharynx, turned dorsally, and then traction may be applied fixing the hook in bones dorsal to the pharynx.

The long blunt hook may be used to advantage in the hiplock condition in anterior presentation. The hook is passed over the top of the fetal croup and turned ventrally to engage the posterior border of the ischium or sacrosclatic ligament. In this position much traction may be applied. By raising the fetal pelvis and pulling the fetal hips at an oblique angle through the maternal pelvis, the veterinarian can often relieve the dystocia.

In ewes, does and sows the obstetrical chains are too large to be of value. In anterior presentation snares or forceps are applied to the ovine or porcine fetal head, around the neck, or to the forelegs. In small sheep and swine, in which the hand cannot be passed through the pelvis into the uterus, forceps of various types, as well as obstetrical snares, may be used to advantage.³⁵ Whenever forceps, snares or chains are applied, the wall of the genital tract should be examined before traction is applied, to make sure it is not caught. In bitches and

queens forceps may be applied to the head of the fetus after the head is repelled out of the pelvis into the uterus; but great care should be used to prevent tearing an ear or lacerating the skin, fracturing the mandible, or crushing the skull. Excessive traction or twisting of the head should be avoided, since injury or dislocation of the vertebrae may occur in the occipital region in these small species. Forced extraction in multipara is limited to those fetuses which have entered the uterine body or pelvis. Snares of gauze may be used on the limbs of canine fetuses. The use of forceps in dystocia in dogs has been described.^{14,25}

In posterior presentation in large animals traction may be applied to the fetal pastern or above the hock by the use of obstetrical chains. The same danger exists as in the anterior presentation whereby excessive traction with chains fastened above the fetlocks or that slide down over the coronary band of the hoof, may cause fracture above the fetlock or removal of the hoof. In ewes and sows, snares may be fastened around the hind legs of the fetus. In bitches and queens snares or gauze around the hind legs or grasping the hocks with sponge forceps will assist traction. If forceps are used in multipara they should be fastened securely around or across the fetal pelvis, after the fetal hips have been repelled out of the maternal pelvis. In bitches, forceps are generally preferred to applying excessive traction to the hind legs with the accompanying possible danger of dislocating the fetal hips. Excessive twisting of the fetal pelvis by the means of forceps may injure the lumbo-sacral articulation; or if the fetus is emphysematous excessive traction may pull it apart. Dislocation of the first cervical joint may occur in posterior presentation in the bitch when the occiput becomes impacted in the pelvis and traction is continued. In this instance abdominal pressure by the operator's hand will raise the chin of the fetus and help force the fetal head through the pelvis.

Technique of Withdrawing Fetus Through the Maternal Birth Canal—In anterior presentation of the fetus in uniparous animals, traction should be applied at three points, the two legs and the head. After the limbs followed by the head have passed through the vulva, traction may be applied to the legs only. At the beginning of labor the main portion of the fetus is below the level of the brim of the pelvis. Traction when applied in either anterior or posterior presentation should be dorsally and caudally to lift the fetus up and over the brim of the pelvis into the birth canal. At this stage, with the fetal extremities approaching the vulva, the direction of traction should at first be caudal and slightly dorsal; and as the fetal legs and head engage in the vulva the direction of traction should be obliquely ventral. After the

head in anterior presentation or the hips in posterior presentation pass through the vulva, the direction of traction should be more and more ventral until when the back of the fetus is passing through the vulva the direction of traction is perpendicular to the spinal axis of the dam or parallel to her hind legs. Thus the direction of traction and that of the fetus as it passes through the birth canal is in the form of an arc. The ventral structures of the fetus are relaxed and concave, and the dorsal structures of the fetus are stretched and convex. This arc-like application of traction results in the fetus assuming the physiologic curved shape that facilitates its removal through the birth canal; by producing the smallest possible diameters of the fetal body stalling of the fetal pelvis, or the hiplock condition, is prevented. By applying traction to the legs, head, and spine the abdominal wall of the fetus is relaxed and the fetal pelvis is forced backward and upward reducing its sacro-pubic diameter and causing it to pass through the greatest diameter of the maternal pelvis. If traction is applied in a straight caudal direction and not in the form of an arc, both the linea alba as well as the spine are stretched, and the fetal pelvis is pulled ventrally and cranially thus increasing its sacro-pubic diameter and predisposing to hiplock. As described previously the rotation of the fetus in the birth canal into the dorsoilial position to cause the fetal pelvis to enter the maternal pelvis at an oblique angle corresponding to the greatest diameter of the maternal pelvis combined with lateral traction often prevents the hiplock condition.^{3,39a} After the fetal hips have been withdrawn through the maternal inlet in an oblique or dorso-ilial position, the fetus should be rotated back to a dorso-sacral position before further traction is applied.

When the head enters the vulva, if traction is applied dorsally or caudally instead of ventrally the fetal head jams against the dorsal commissure of the vulva and may cause severe stretching or laceration. At this point it is important to place ventral traction on the head. When the vulva is small, especially in primiparous cattle, ventral traction on the head alone together with insertion of the hands over the top of the head; stretching of the vulva with the wrists, arms or hands; and ventral and caudal traction with the hands over the occiput or with the fingers in the medial canthus of the orbit helps to pass the head through the vulva and prevent lacerations. Often, if this process is prolonged, lubrication of the head and vulva is helpful. Pushing or pulling cranially on the vulva if the vulva is tight while traction is applied on the fetal head will further aid dilation.

When abdominal contractions in the dam occur during parturition the linea alba pulls the pubis forward, increasing the pelvic diameters. When strong traction is

applied to the fetus and the pelvic ligaments are relaxed the maternal pubis is pulled caudally and the pelvic diameters are lessened. A rope or breeching around the buttocks of the cow in lateral recumbency fastened securely to the manger so that when traction is applied to the fetus the maternal pubis is pulled forward by this rope or breeching was recommended.⁵⁶ The metal breech device used with fetal extractors provides this same advantage. Preventing the maternal pubis from extending caudally, and applying ventral traction on the fetus, will usually prevent impaction of the fetal hips in the maternal pelvis. Improper traction such as that produced by a block and tackle pulling directly caudally will in many instances cause severe impaction of the fetus in the maternal pelvis.

When traction is applied the operator should constantly watch, examine, and direct the progress of the fetus by instructing his assistants when to apply traction, when it should cease, and in what direction it should be applied. If the progress of the fetus through the birth canal should cease, traction should be discontinued and the fetus and the birth canal should be carefully examined to determine the cause of the obstruction. This should be overcome or corrected before exerting further traction. The operator should conserve his strength and direct the operation and not join his assistants in applying traction except when necessary. If the patient is straining, traction should be applied principally during expulsive efforts. This both aids the withdrawal of the fetus and to some extent prevents the fetus dragging portions of the uterus and vagina along with it, thereby causing possible rupture or prolapse of the uterus. Traction should be applied in a steady, even manner. Jerky, irregular efforts at traction are ineffectual, painful and dangerous to both the fetus and dam. In most instances traction should not be applied in a hasty manner. To avoid lacerations or ruptures of the soft structures of the birth canal time should be allowed for dilation of the birth canal as the fetus advances. This frequently requires 30 minutes or longer in heifers. The same general technique of removing fetuses by traction in ewes, sows, does, bitches and queens is followed with traction caudally and then downward as the fetus passes through the vulva. In the bitch and queen pressure of the operator's hand upward through the abdominal wall will help the passage of the fetus into the pelvis and through the birth canal.

In uniparous animals traction may be greatly facilitated by lubrication if the fetus and birth canal are dry. Traction on one extremity at a time in an alternate manner is also of assistance in withdrawing a fetus. This is especially true in posterior presentation, in which traction should be applied to one limb at a time so that the

fetal pelvis is pulled through the maternal pelvis in an oblique manner, thus reducing the possibility of hiplock. Even in anterior presentation, after the forelimbs and head have passed through the vulva, pulling the bovine fetus laterally and ventrally around the dam's hips first to one side and then to the other may aid in withdrawal of the fetus and produce an oblique angle to the fetal pelvis, so that one greater trochanter will slip through the maternal pelvic inlet and then the other will follow, preventing or reducing the chances of hiplock or impaction. As traction is applied, rotating of the fetal body from side to side may aid withdrawal of the fetus.

Indications for Forced Extraction of the Fetus—

Forced extraction is indicated when uterine inertia is present and the fetus does not engage in the birth canal and stimulate straining. It is indicated when epidural anesthesia has been administered and after mutation has corrected the cause for dystocia. Forced extraction is used most often when the fetus is relatively too large to be expelled through the birth canal without assistance, fetopelvic disproportion, and when traction offers greater prospect of success than a fetotomy or cesarean. It is used in many cases in primipara with a small birth canal, as a means of withdrawing the fetus and dilating the canal. It may also be used when the birth canal is compressed by tumors or fat or other pathological conditions. It may be indicated in posterior presentation of the fetus to hasten delivery and prevent the death of the fetus when the umbilical cord is compressed between the fetal abdominal wall and the brim of the pelvis. Within 5 to 10 minutes after the umbilical circulation is cut off the fetus may die if its cranial extremities remain in the uterus and it cannot breathe. Hasty application of forced extraction may occasionally be indicated in mares with dystocia in which the cause for the dystocia has been corrected and the fetus is still alive. Thus it may effect removal of the fetus before separation of the placenta and death of the fetus occur. Forced extraction may occasionally be used to save time or in order to avoid fetotomy or cesarean section where working conditions are extremely poor. It is indicated in dystocia due to emphysematous fetuses after thoroughly lubricating the birth canal and fetus to avoid fetotomy or a cesarean, which are more hazardous to the dam than is forced extraction under such conditions. In many fetotomy operations, forced extraction is used as an aid.

Forced extraction by forceps or snares in the multiparous animals, sow, bitch, and queen, should not be used when one is short of time or patience as it may require a number of hours of intermittent work to complete the delivery of all the fetuses. It is, however, indicated when the owner is not interested in saving the

fetuses; when only one or two fetuses are present and secondary uterine inertia has set in; when the fetuses are dead and emphysematous; and when in the opinion of the operator the delivery of one fetus will result in the unaided delivery of the rest of the litter. The veterinarian may even decide to use forceps and forced extraction in cases of primary inertia where the litter is small. Young primiparous bitches may force the fetal head through the pelvis and then rest. This pup becomes cyanotic and must be delivered immediately. Since the vulva is small and tight it is necessary to force the pup's head through by means of outside pressure on the vulvar lips. Then by applying manual traction on the head and placing a finger under the pup's chest, the pup can be eased through the vulva.²⁵ To prevent the fingers from slipping, a gauze pad may be used.

Forced extraction should be limited strictly to cases in which the presentation, position and posture of the fetus are normal and in which, in the opinion of the operator, forced extraction is in the best interests of the fetus, the dam and the owner. Forced extraction is contraindicated or should only be undertaken with great care when abnormal presentation, position or postures are present, when the fetus is excessively large or defective, when the birth canal is obviously small, when the animal is affected with obturator paralysis, when the birth canal has been severely lacerated, when secondary uterine inertia is present with the uterine walls strongly contracted around the fetus, and when the cervix is stenotic or has failed to dilate. In these latter conditions uterine relaxants and spasmolytic drugs might be recommended.² However, these products for use in dystocia in animals in the U.S.A. are not currently available.

The Amount of Traction to Apply in Forced Extraction of the Fetus will vary greatly with the species of animal and the condition causing the dystocia. Although forced extraction appears simple and quick it is potentially dangerous to the fetus and to the dam. In the dam, excessive traction or traction in an improper manner or with the fetus in an abnormal presentation, position, and posture may result in trauma, laceration, rupture to the soft structures of the birth canal or uterus or wedging of the fetus in the dam's pelvis. It may predispose to prolapse of the uterus, or result in trauma to the obturator or gluteal nerves. However it is remarkable how seldom paralysis occurs even when excessive traction has been applied.

In the mare, abdominal contractions are so violent that if the fetus is in the proper presentation, position and posture, forced extraction is seldom necessary. Aid with obstetrical chains by one or two men may help dilate the birth canal and vulva gradually in old or young primi-

parous mares. Care should be exercised to avoid lacerating the vulva or the perineal region. If the mare is recumbent and much traction is applied, she will usually get to her feet. If the cow is standing and strong traction is applied to the fetus, the cow will usually fall and may injure itself or the attendants. In the cow, as in the mare, traction under certain circumstances should be moderate and intermittent; for example, if the fetus is alive and the cow already exhibits some obturator paralysis due to a hiplock condition. In normal circumstances the force of 2 to 3 men apparently causes no harm and may be indicated. The introduction of the fetal extractor with which one can exert great force in the proper manner, if necessary, has been received enthusiastically by many veterinarians because often sufficient manpower is not available and the block and tackle or wire stretchers previously used applied traction in only one direction and in an improper manner, that is, directly caudally. Since excessive power can easily be applied by the fetal extractor, judgment, caution, and care must be exercised in its use. Where great amounts of traction are used, epidural analgesia is strongly recommended to avoid excessive pain in the dam. The amount of traction to be applied will vary from case to case and with the judgment of the veterinarian. Following forced extraction of large fetuses of beef cattle including Charolais, Charolais-cross and Simmental-cross calves, both hard and soft tissue injuries have been reported.^{17a,30} The hard tissue injuries include; fractures of the proximal end of the femur and slipped capital femoral epiphysis,^{17a} fractures of the ribs, costo-chondral junctions, lumbar vertebrae and metacarpal or metatarsal bones. The soft tissue injuries include: femoral nerve paralysis and quadriceps femoris muscle damage and atrophy due to hyperextension of the femur.⁴³ The author has observed that the above injuries to the newborn are much more common with the recent increased breeding of the exotic beef crossbreds and the introduction of the fetal extractor often employed by farmers or ranchers to relieve dystocia. Traction if properly applied seldom results in injury to the fetus or to the genital tract of the mare and cow. However, to quote Williams,⁵⁶ "Application of great force in improper position, presentation or posture of the fetus is constantly to be condemned." The use of a tractor or horses to apply traction to the fetus, or tying the fetus to a tree and driving the parturient mare away, are definite examples of malpractice if performed by a veterinarian.

In the ewe, doe and sow the same principles in regard to the degree of traction may be applied. In all cases, however, the force exerted by one man is sufficient for the relief of dystocia in these species. In the ewe and doe, before applying traction one should make certain

the snare is attached to one, not two, fetuses. In bitches and queens traction should be applied carefully and never excessively. Twisting of the fetus should be avoided. Occasionally in emphysematous fetuses traction may pull the fetus apart. In these small species traction should be used with care, especially if secondary uterine inertia has set in, to avoid laceration of the uterus or birth canal at the pelvic brim. This will result in herniation of the viscera through the birth canal or discharge of the fetuses into the abdominal cavity.

Fetotomy

Fetotomy is defined as those operations performed on the fetus for the purpose of reducing its size by either its division or the removal of certain of its parts. In most cases these operations are performed within the uterus of the dam. Partial fetotomy is most commonly performed. Total fetotomy is performed infrequently. In fetotomy the life of the fetus is sacrificed if it is not already dead as is usually the case. In Germany attention has been paid to humane methods of killing the fetus, before fetotomy is begun.⁴ These authors indicate the fetal reflexes and threshold for pain are of a very low order. For this reason incising the carotid artery or rupturing the umbilical cord before fetotomy is not necessary. The injection of a rapid-acting drug to produce euthanasia or an anesthetic state in the fetus has not been investigated but any such agent might well be transferred by the placenta to the dam.

If the fetus is dead and the birth canal is not reduced in size, fetotomy should be given primary consideration.⁵⁹ The **advantages of fetotomy** are: It reduces the size of the fetus. It avoids a cesarean operation. It requires little assistance. It will prevent possible trauma or injury to the dam through the use of excessive traction.^{2,5,7,59}

The **disadvantages of fetotomy** are: It may be dangerous, causing injuries or lacerations to the uterus or birth canal by instruments or sharp edges of bone. It may take a long time, exhausting both the dam and the operator and is conducive to trauma and pressure necrosis of the birth canal. It offers certain dangers to the veterinarian by wounds from instruments, and if the fetus is emphysematous there is a possibility of infection of the skin of the operator's arms.

The advantages outweigh the disadvantages, however, and fetotomy in large animals is a practical and successful way of relieving dystocia. It is used, and rightly so, many more times than is cesarean section, which is more costly and time consuming, and requires more help

and more aftercare than do most fetotomy operations. Cesarean section is indicated over fetotomy only if the fetus is alive and the owner desires that it be saved; or when total fetotomy under difficult conditions, such as a small narrow birth canal, would probably cause greater trauma to the dam, take longer, and be more fatiguing to both the dam and veterinarian than would cesarean section. If there is little prospect of a successful fetotomy operation and forced extraction is impossible, the owner should be advised to have a cesarean operation performed or to slaughter the dam.

Since cesarean section is more difficult to perform successfully in the mare than in the other domestic animals, fetotomy or forced extraction are methods of choice in this species. Because the genital tract of the mare is more easily traumatized, and with more serious consequences than that of the cow, fetotomy should be performed carefully and gently. For more than a simply fetotomy in the mare, a general anesthesia should probably be administered. The mare should be restrained in a suitable location large enough for the operation to be performed with the mare lying on her side.

Simple fetotomy techniques using a guarded obstetrical wire² may be performed in the ewe and doe if the hand can be passed through the pelvis into the uterus. By threading a loop of the obstetrical wire through a pipe of small diameter, portions of the fetus, such as the head and forelimbs, may be removed with safety to the dam. Fetotomies are not performed in the sow, bitch, and queen because cesarean section is easier and safer. In rare cases in the bitch the skull of the fetus may be crushed intentionally by means of forceps in order to permit removal by traction.

Vandeplassche and his associates^{48,49,50} compared the results of 239 fetotomies and 150 cesarean operations in cattle and came to the conclusion that fetotomy was still the more important and practical of the two methods in bovine veterinary practice. In summarizing the data on these 239 cases it was found that in 3 to 5 percent of them fetotomy was impossible. Six percent of the cows died, 6 of them from septic metritis, 2 from malignant edema, 3 from necrotic vaginitis, 1 from a ruptured uterus, and 1 from hemorrhage. Thirteen percent of the cows had retained fetal membranes and 82 percent conceived within 10 months after the fetotomy operation. A more recent review of the literature reported on many hundreds of fetotomy and laparohysterotomy (Cesarean) operations and indicated that both procedures have their place in veterinary obstetrics.⁵⁹

The fetotomy operation may involve any portion of the fetal body and presents many variations and possibilities. It may be performed in any normal or abnormal

presentation, position, or posture of the fetus. In many cases it is employed in relieving dystocia due to fetal monsters in which the usual anatomical arrangement of parts may not exist. The operational procedure must be decided upon for each case. Fetotomy operations should be planned and carried out carefully, so that there will be no wasted effort. Generally, by careful planning and by using mutation or forced extraction, only one fetotomy operation, instead of two, may be necessary. It should be borne in mind that the aim of fetotomy is to reduce the size of the fetus so it may be removed from the birth canal. The veterinarian therefore should, depending upon the particular conditions and circumstances, plan the operation and procedures using one or more of the standard fetotomy operations or their variations. At the present time the fetatome is standard equipment for the practitioner working with large animals; therefore many of the older techniques⁵⁶ using instruments such as the knife, chisel, and blunt-pointed cutting hook are not often used. These older techniques, using simple instruments, involved some operations which were difficult to perform, requiring patience, strength, and extreme effort, placing a severe strain on both the operator and the animal. Veterinarians who have become adept through practice may perform many obstetrical operations with the knife, chisel, and hook and seldom use the fetatome. The author has for many years been a staunch advocate of the fetatome primarily because it is easier and safer to use. Except for minor simple obstetrical operations, he prefers it to the older instruments and their accompanying techniques. Some of the simpler older techniques are still practical, however, and will be described.

In dairy cattle practice in New York State 90 percent of the fetotomy operations performed include: bisecting the pelvis in anterior presentation, (hiplock) or in posterior presentation, (breech presentation), amputation of the head and neck, and decapitation. In some cases evisceration is used prior to bisecting the pelvis in anterior presentation.

Presently many of the subcutaneous fetotomy techniques advocated by Williams and others⁵⁶ are rapidly declining in popularity. The newer percutaneous techniques pioneered by the Utrecht clinicians with their modification of the fetatome are being rapidly accepted and utilized because of their ease and safety of application.^{5,4,59}

Fetotomy Operations in the Anterior Presentation

Decapitation, or Amputation of the Protruding Head is indicated when one or both forelimbs are retained and

the head has passed through the vulva and become swollen, edematous, or emphysematous so that it cannot be repelled or can be repelled only with great difficulty. In such cases the fetus is usually dead, and amputation of its head allows the fetus to be repelled, so that the abnormal posture of the forelimbs may readily be corrected by mutation, without the interference of the head.

Decapitation is easily accomplished by fixing a snare on the lower jaw, or eye hooks in the orbits, and exerting traction in any direction desired by the operator. With a scalpel or sharp knife a transverse incision is made behind the jaw through the skin, muscles, pharynx, larynx and esophagus to the cervical vertebra. This incision is continued through the skin ventral to the ears and across the frontal bones. The skin over the head, including the ears, is separated from the underlying muscle and bone to the occipital region, where another transverse incision is made ventrally through the ligamentum nuchae and muscles to the cervical vertebra. The head is grasped firmly and twisted, rupturing the articular ligaments. The remaining soft tissues are cut and the head removed from the neck at the occipital atlod articulation. The flap of skin, including the ears, should be firmly secured by an obstetrical chain or snare which pulls the skin over the exposed cervical vertebra. A small incision in this flap of skin distal to the loop of obstetrical chain and through which the free end of the chain is drawn will secure the chain so it cannot slip off even if strong traction is applied. The fetus is then repelled, and the abnormal posture of the limbs corrected by mutation. Traction on the neck and two front legs usually results in relief of the dystocia. In making the incisions the operator must guard against the knife accidentally slipping and cutting the vulva. The fetatome could also be used in this operation, but the technique just described saves time as well as aftercare of equipment.

Cephalotomy or craniotomy is indicated only rarely when fetal hydrocephalus or other cranial deformity is the cause for dystocia.

Cephalotomy is accomplished by fixing the head with a snare around the lower jaw or chain attached to Krey's tongs inserted in the orbits. In hydrocephalus sometimes simply incising the distended cranium causes a sufficient reduction in size to permit delivery. In most cases, however, it is necessary to separate the enlarged cranium from the rest of the head by passing the wire of the fetatome around its base. With the fetal head fastened under tension to the chain fixation plate on the handle of the Utrecht fetatome and its head against the base of the enlarged cranium it is readily severed. Then the collapsed cranial bones and skin may be removed. The rest of the fetus can be withdrawn unless this is prevented by ankylosis

of the joints, a common characteristic of the hydrocephalic fetus.

Amputation of the Head and Neck is indicated when the head and neck are retained alongside, beneath, or above the body of the fetus or when performing a complete fetotomy.² Correction of this abnormal posture by mutation may be impossible or extremely difficult or dangerous, due to such conditions as wry neck, a uterus contracted tightly around the fetus, or to a dry, emphysematous fetus. Amputation may possibly be indicated when, due to a juvenile or hypoplastic pelvis or to a large fetal head, there is not room in the birth canal for the simultaneous presence of the head and neck and the two limbs. If this condition is present, one should determine accurately the relative size of the fetus and the birth canal because, if after removal of the head and neck further operations such as a total fetotomy are necessary, cesarean section might be preferable.

Amputation of the head and neck may be performed by the wire saw or fetatome. The latter is preferred because if the operation is performed properly the neck is amputated close enough to the body so that traction of the forelimbs will pull the scapulas and shoulder joints over the exposed stump of the neck vertebrae. Occasionally in a large mare it may be necessary to remove the forelimb opposite the side to which the head and neck are flexed, and to apply traction to the fetus in order to enable the operator to reach the neck and pass the fetatome wire around it. With the aid of the fetatome wire guide or obstetrical chain the fetatome wire is threaded over the base of the flexed neck and drawn around it. The head of the fetatome is held forcibly between the shoulder joint and neck of the fetus and the neck is severed as close to the body as possible. The neck and head are then withdrawn by means of the hand, a snare, or Krey's hooks. Traction on the forelegs of the fetus will deliver the fetal body unless further operations must be performed. If the cervical stump is long, it must be guided with Krey's tongs and guarded with the hand to prevent possible laceration of the birth canal as the fetus is withdrawn.

Amputation of the Forelimb is indicated to provide space so that amputation of the head and neck may be possible or easier. If the foreleg is retained or extended beneath the body and mutation is not possible due to fetal emphysema or contraction of the uterine wall, amputation of the foreleg is necessary. It is indicated in large or emphysematous fetuses to reduce their size and expose the ribs for evisceration. In rare cases it may be indicated in transverse ventral presentation in the mare in which after amputation of the two hind legs at the tarsus, and the underneath foreleg at the humeroradial

joint, the upper front leg may be removed in the manner described below and evisceration performed, if necessary, before the fetus is corrected by version into a posterior presentation.

Amputation of the forelimb is initiated by means of constant traction applied to the leg with a snare or obstetrical chain. By making a crescent-shaped incision through the skin of the fetus and its trapezius and rhomboideus muscles dorsal to the scapula with a hoe-bladed castrating knife or other knife, the dorsal end of the scapula is separated from the body. A loop of fetatome wire is placed around the limb and moved up the limb as the head of the fetatome is placed in the pectoral region. The wire loop is then moved upward and placed in the incision under the cartilage of the scapula, and the limb removed. This technique is particularly adapted to the cow; it is more difficult to perform in the mare due to the longer limbs of the equine fetus.

Another technique is that of placing the loop of fetatome wire around the limb to be removed while the head of the fetatome is placed just dorsal and caudal to the top of the fetal scapula. The limb is extended tautly, by traction by a chain to the chain plate on the handle of the Utrecht fetatome. By means of acute-angled sawing the limb is removed. The wire usually passes through the dorsal part of the scapula. On occasion one forelimb as well as the head and neck can be removed in a like manner by proper placing of the wire to include the head and neck. The removal of the forelimb extended beneath the body is easily performed by passing the fetatome wire behind the elbow and beneath the arm. By placing the head of the fetatome on the withers of the fetus, the entire limb can be removed rapidly.

The above two methods of amputation of the forelimb removes the skin over the chest wall, so that if evisceration is performed the broken ends of the ribs are not covered. The older techniques of **subcutaneous amputation** of the forelimb with a knife and chisel are relatively simple and rapid, especially when the fetus is emphysematous.^{2,37a,56} They are seldom performed however because the use of the fetatome is more rapid and less stressful to the dam and operator. In fetal emphysema the muscles are greatly weakened. In many such amputations the fetal extractor is useful. For example one may girdle the skin above the knee, apply the extractor and rapidly remove the entire limb.

Amputation of the Anterior Limb at the Humero-Radial Articulation is indicated in the removal of the forelimbs in rare transverse ventral presentations in the mare prior to version of the fetus into a posterior presentation. Amputation of the entire forelimb is difficult or impossible in this presentation. Amputation at the hu-

mero-radial articulation is accomplished by exerting traction on the limb. A loop of fetatome wire is placed around the leg and the head of the fetatome is pushed ahead of the wire loop to the pectoral region and held there firmly while the wire loop is passed up the leg and over the olecranon and tightened around the leg. The handle of the fetatome may be fastened by a chain or held securely to the extended leg in the metacarpal region, preventing the head of the fetatome from slipping downward as the leg is amputated through the distal end of the humerus. The other limb is removed in a similar manner.

Evisceration in Anterior Presentation is indicated to reduce the size of a large or emphysematous fetus and make it less inflexible, or to release ascitic fluid in fetal ascites. It may be indicated to assist the operator in putting his arm through the birth canal to thread the fetatome wire around the pelvis in hiplock in anterior presentation. It is also helpful in rare cases if the ribs are to be broken down for further reduction of the size of the thoracic or pectoral girdle.

When the fetus is within the birth canal or uterus, evisceration in anterior presentation may be performed by amputation of the forelimb including the scapula with a fetatome which exposes the ribs. The intercostal muscles between the first, second, third, fourth, and fifth ribs are separated by the finger or knife from the spine to the sternum. In order to gain free access to the thoracic and abdominal cavities, the second, third, and sometimes the fourth ribs are removed by cutting the costal cartilage just above the sternum with a knife, chisel, or cutting hook and bending the rib dorsally to break it off next to the spinal column, or with a cutting hook or chisel cutting the rib loose as near the spine as possible. If the cutting hook and chisel are used they should be carefully guided and guarded by one hand of the operator while controlled traction or thrusting motions are provided by the other arm, so that the uterus or birth canal are not injured by slipping of the instrument. The ribs should not be broken in the middle as it is difficult to remove both ends, especially the ventral part, and the broken ends are likely to lacerate the operator's hand or arm. The heart and lungs are removed by manual traction after grasping the heart at its base and clasping the fingers firmly around the large vessels. By grasping the lungs in the region of the bifurcation of the trachea first one and then the other or both lungs can be removed. After the thoracic viscera have been removed the fingers are thrust through the diaphragm in the region of the large vessels and the opening enlarged. The stomach and intestines are easily removed by wrapping them around the hand. The liver, the largest organ to be removed, is pulled

loose from the diaphragm and withdrawn, usually in several pieces. The kidneys are small and therefore need not be removed.

Destruction of the Rib Cage—On uncommon occasions, to further reduce the size of the thorax, the remainder of the ribs may be broken down with the cutting hook or the chisel. If the blunt-pointed cutting hook is used, the hook is pushed caudally between the skin and ribs about midway between the spine and the sternum until the end of the hook passes beyond the last rib. The point of the hook is turned medially through the abdominal wall and by short, firm pulls the hook is drawn through one to two ribs at a time until only one rib remains to be broken. To avoid cutting this rib suddenly and having the hook tear out of the fetus and possibly injure the uterus or the operator's hand, this last rib may be broken by twisting the hook instead of applying traction. If necessary the ribs on the other side of the thorax may be broken down by introducing the cutting hook through the body cavity to the last rib turning the point outward through the abdominal muscles and pulling the hook back through the ribs in the manner described above. Since the point of the hook is under the skin and might catch it or cut through a fold of skin, the operator's hand outside the skin should guard and follow the progress of the hook. Another technique is to make a 3- to 4-inch vertical incision through the skin cranial to the opposite shoulder and push the cutting hook along the outside of the ribs beneath the shoulder and skin to the last rib and, turning the point of the hook medially, cut through the ribs as was done on the first side after the foreleg had been removed and the fetus eviscerated. A chisel instead of the blunt cutting hook may be used for breaking the ribs in a fetus fixed in the birth canal by traction.

Complete percutaneous Fetotomy in the Anterior Presentation—Since evisceration and breaking down the fetal ribs is difficult especially in a cow with definite fetopelvic disproportion, a complete percutaneous fetotomy in anterior presentation as described by Bierschwal and de Bois and others using the Utrecht model fetatome may be easier.^{5,4,59} This technique requires amputation of the head; amputation of both forelimbs, including the scapulas; transverse division of the anterior chest or trunk; transverse diversion of the posterior portion of chest through the abdominal wall caudal to the last rib; and bisection of the fetal pelvis through the sacrum and pubis. If the posterior portion of the chest or rib cage is of too great diameter to be withdrawn easily, the ribs are severed longitudinally by the fetatome near their vertebral attachment.

Detruncation in Anterior Presentation is indicated in rare instances when the fetus is in a "dog sitting" pos-

ture with the hind limbs extended alongside or beneath the body and wedged into or against the maternal pelvis. If repulsion and mutation are impossible due to protracted dystocia, or if the head and forelegs are outside the vulva, fetotomy is usually necessary.

To perform detruncation by means of the fetatome, a loop of fetatome wire is passed around the body of the fetus and the head of the fetatome is inserted into the birth canal over the lumbar region of the fetus. After the wire is manipulated back of the last ribs, detruncation is rapidly accomplished. On occasions two cuts through the trunk of a large fetus may be necessary. Using Krey's tongs on the exposed vertebrae for traction further reduction of the fetal body is facilitated. Evisceration would make this operation safer and easier if the fetus is large or emphysematous, or if the birth canal is swollen, small, or dry. Lubrication to prevent trauma to the birth canal is essential. Following detruncation, chains are applied to the two hind limbs and by traction on the limbs and repulsion on the spine the hind quarters of the fetus may be turned to a posterior presentation dorso-pubic position. After the hind quarters have been rotated to a dorso-sacral position they are removed by traction. If the pelvis of the fetus is large, its bisection with the fetatome should be considered without attempting mutation.

Bisection of the Pelvis in Anterior Presentation is commonly indicated when the fetal pelvis becomes wedged in the maternal pelvis. In these cases the bisiliac diameter of the maternal pelvis is smaller than the distance between the greater trochanters of the fetal hips thus causing hiplock. When this has existed for a number of hours as a cause of dystocia one should examine the cow carefully, since symptoms of obturator paralysis are present in many such cases. If symptoms of obturator paralysis are present, bisection of the fetal pelvis is indicated in preference to forced extraction to prevent further trauma to the obturator nerve. When the hiplock condition cannot be relieved by lubrication, mutation and traction, fetotomy is necessary.

This may be performed with the fetatome. In using the fetatome, the wire is passed over the top of the fetal pelvis and as far down as possible behind the ischial arch. By passing the hand under the fetus and fetal pelvis the introducer, threader or obstetrical chain which is attached to the wire is pulled between the hind legs. After placing this end of the wire through the fetatome, the head of the fetatome is placed alongside the body of the fetus opposite the ribs. If the loop of the wire is on the right side of the tail the head of the fetatome should be on the left side of the fetus so the fetatome wire passes through the middle of the pelvis and not through the head of the femur. After the pelvis is bisected, the fetus minus

one hind leg can be removed; then if the operator grasps the exposed pelvic bones the other hind leg can be withdrawn. This operation is made easier by evisceration, which allows the operator more room in the pelvic cavity for placing the wire and the fetatome in position.

A simple procedure combining forced extraction, evisceration, and bisection of the pelvis is frequently used by the author to relieve dystocia in heifers with fetopelvic disproportion. By means of forced extraction with the fetal extractor, the well-lubricated fetus is pulled through the birth canal until the hips approach the maternal pelvis. In rare instances it may be necessary to amputate the head and neck or the head, neck and one forelimb in order to accomplish this. The forequarters outside the vulva are pulled dorsally, exposing the umbilical region of the fetus. The abdominal wall is cut transversely and evisceration is easily completed through this wide incision. In many cases this incision extends dorsally through the intercostal muscles of one of the last 2 to 4 ribs, but these are short and cause no problem. If the difference between the size of the maternal and fetal pelvis is not relatively great, traction is once more attempted. The long blunt hook is passed over the top of the pelvis and hooked on the ischial arch or into the caudal border of the sacro-sciatic ligament, providing a firm hold for traction and for elevation of the fetal pelvis. This also causes the fetal pelvis to be turned obliquely, thereby facilitating delivery. Since the abdominal wall has already been cut, and evisceration has greatly reduced resistance in the birth canal and all the traction is on the fetal spine, correction of the dystocia in many such cases can be accomplished without bisecting the pelvis. Mutating the fetus into a dorso-iliac position before applying traction may assist in the removal of the fetus by traction without bisecting the pelvis with the fetatome.

Fetotomy Operations in the Posterior Presentation

Fetotomy in Normal Posterior Presentation is indicated when the diameter of the fetal pelvis is relatively larger than the diameter of the pelvic inlet and wedging or hiplock occurs. This condition is seen usually in immature or stunted heifers and may be complicated by an emphysematous fetus. Under these conditions cesarean section or slaughter may occasionally be advisable.

Fetotomy consisting of the amputation of one leg, or preferably one leg and part of the pelvis, may be accomplished by means of the fetatome. A transverse incision just cranial to the external wing of the ilium is made in the fetus through the skin and muscle. A loop

of fetatome wire is carried up the hind leg and placed in this incision. The head of the fetatome is placed between the hind legs. One hind leg and a portion of the pelvis are removed. A variation in this technique consists of passing the loop of fetatome wire around both legs and over the hips to the lumbar region of the fetus. With the head of the fetatome on one hip a cut is made with the wire halfway through the lumbar region just cranial to the fetal pelvis. The head of the fetatome is pulled outside the cow and reinserted to rest between the two legs of the fetus and the rest of the cutting is completed, bisecting the fetal pelvis longitudinally. Another technique is that of acute angle sawing with the fetatome.^{3,5} The loop of wire is placed around one leg and the head of the fetatome is placed dorsal to the wings of the ilium or even in the caudal lumbar region. The leg is tautly extended and fastened to the handle of the fetatome outside the dam to insure a portion of the fetal pelvis being included with the amputated limb. Often, the leg is amputated through the hip joint because it is difficult to hold the head of the fetatome in place.

Bisection of the Pelvis in Breech Presentation is indicated in posterior presentation in uniparous animals with the hind limbs of the fetus extended or retained beneath the body, when dystocia has been present for some time, the uterus is contracted, the fetus emphysematous, and the uterus and birth passages are dry and swollen, so that mutation is difficult or impossible.

The fetatome may be used in this operation. The heavy metal guide, introducer, or obstetrical chain is securely fastened to the fetatome wire and then introduced through the birth canal and over the thigh of the fetus between the leg and abdomen. It is pushed as far as possible ventrally and caudally. The hand is then passed beneath the fetal pelvis and between the legs and the wire is drawn out through the vulva. The threaded fetatome is placed on the hip opposite the leg to be removed; that is, if the wire loop is around the right leg of the fetus the head of the fetatome should be on or just behind the greater trochanter of the left leg to insure a large portion of the pelvis being removed with the leg. If the head of the fetatome is not firmly held in place it will pull directly caudal to the perineal region and the leg will be removed at the hip joint or proximal end of the femur. After the leg and portion of the pelvis is removed the rest of the fetus can usually be withdrawn by traction on the pelvic bones with the long blunt hook or Krey's hooks, with the opposite leg still extended alongside the body. If this is not possible, the operation may have provided enough room to correct the posture of the remaining limb by mutation. In rare cases evisceration may be performed to assist in the removal of the fetus.

Another method of reduction of the pelvis in breech presentation is to place a loop of fetatome wire in a fetatome around the presenting buttocks. The head of the fetatome is placed in the region of the fetal lumbar vertebrae and held in place by an obstetrical chain tightly fastened to the handle of the fetatome and by Krey's tongs to the fetal sacrosciatic ligament or sacrum. By acute angle sawing, this removes most of the pelvic bones and tail and may permit withdrawal of the fetus with both limbs alongside the body.

Amputation of the Rear Limbs at the Tarsus may be indicated in rare instances in the mare in order to obtain additional room for removal of the forelegs in transverse ventral presentation, in cases in which the metatarsal bone is wedged into or across the pelvis, or when mutation of a hock-flexed posture in a mare is impossible. It may occasionally be necessary in monsters with ankylosed hind limbs, such as *Perosomus elumbis*.

The operation is easily performed by slipping a loop of fetatome wire around the leg. The head of the fetatome is placed on the lower row of tarsal bones or the head of the metatarsal bone, and the leg is cut off in this region. Thus the lower portion of the limb is removed and the os calcis is left attached. The obstetrical chain will find secure lodging above this point when traction is applied.

Evisceration and Breakdown of the Ribs in Posterior Presentation is indicated when further reduction in the size of the trunk is desired in order to effect removal of the fetus.

After removal of one or both of the posterior limbs the opening into the abdominal cavity may be enlarged and the viscera removed as described under evisceration in anterior presentation but in a reverse manner, removing first the abdominal and then the thoracic viscera. The ribs may be broken down in the manner described previously, using the blunt-pointed cutting hook or chisel, but in the reverse order. In certain cases in which it is necessary to break down the thoracic cage after evisceration, the fetatome wire might be passed cranial to the shoulder and between the front legs, thus bisecting the thorax.

Other Fetotomy Operations

There are many other fetotomy operations that may occasionally be used to relieve dystocia. Some are variations of those just described. In fetal monsters causing dystocia, fetotomy operations must be designed to fit the individual case, using the basic operations and principles as a guide. In these cases fetotomies should be planned

carefully and in a manner to reduce the number of cuts to a minimum. Double monsters or those single monsters that are sharply bent, such as *Schistosomus*¹⁸ and *Cam-pylorrhachis*, should be divided as nearly as possible into two equal sections so that removal may be prompt and easy. One should not attempt to start a fetotomy operation without being quite certain that the dystocia can be relieved by the planned operation. In many cases consultation may be advisable. It should be borne in mind that a prolonged unsuccessful fetotomy will make the prognosis more grave if the operator finally attempts to perform a cesarean section.

Ischio-pubic Symphysiotomy—A simple, rapid, technique for splitting of the maternal pelvis at the symphysis pubis in immature or stunted beef heifers under 24 months of age suffering from dystocia due to a small pelvic inlet has been described.^{6,10,16,19} To facilitate securing a live calf, one could induce parturition within the last 2 weeks of gestation with dexamethasone (30 to 60 mg). It is interesting that a brief notation of this symphysiotomy technique was described in a French book in the nineteenth century.⁶ This operation is preferably done on a standing heifer. Epidural anesthesia is administered. One authority recommends passing a metal catheter into the bladder to monitor the location of the bladder before, during and after the symphysiotomy and using a small hypodermic needle to punch through the vaginal floor to ascertain before the operation that there are no areas of ossification in the symphysis.⁷ The area beneath the vulva is washed, shaved, and disinfected. In as aseptic a manner as possible a 4 cm incision is made through the skin and down the exact midline to the ischial arch avoiding the perineal vessels which can bleed profusely if incised. A small, guarded obstetrical chisel* is driven slowly into the symphysis, guided by the operator's hand in the vagina, and the pelvis is carefully split. The chisel should be pushed back and forth through the symphysis several times to separate any fibrous attachments. Traction is applied to the fetus. Because at the time of parturition the ligamentous structures are relaxed, the pelvis spreads 2 to 3 inches and allows the fetus to be withdrawn by manual traction or by the fetal extractor. Aftercare consists of keeping the heifer quiet, isolated and confined for several days or longer. Although the heifer may show some stiffness and slowness of gait it is able to get up and walk. Mounting by other cattle should be avoided. If symptoms of obturator paralysis are present it is advisable to tie a bowline around each hind fetlock with about 18 to 20 inches of rope between them. This

is removed in about 1 to 3 days if the animal can handle itself well. Parenteral antibiotics are given to control possible infection at the operative site. By this technique fetotomy and cesarean section are avoided. Although this practice may be acceptable for beef cattle in some of the range sections of the West, eastern dairymen and veterinarians would be reluctant to accept it for dairy heifers. This operation should not be performed on fat heifers or older cows. This technique of symphysiotomy has also been used successfully in yearling ewes to avoid a cesarean section.¹⁶ Occasionally in heifers a large calcified callus will form if the pubis bone is damaged. This might interfere with subsequent calvings.

Aftercare and Examination of the Dam after Mutation, Forced Extraction, or Fetotomy

Following a dystocia operation the genital tract should always be examined for the presence of another fetus in the uterus or abdominal cavity. This can readily be determined in the mare, cow, doe and ewe if the hand and arm can enter the uterus. It can be very embarrassing to a veterinarian to apparently relieve a dystocia only to be called back again in 2 to 4 hours or later for another dystocia in the same cow. Occasionally the second fetus may not be found until 2 to 3 days later when the cow develops anorexia, tenesmus, or attempts are made to remove a retained placenta. In the sow the farrowing of the last fetus is usually followed by the sow becoming quiet and content, nursing her pigs, urinating, eating, and drinking. If the sow remains restless, uneasy, shows anorexia and intermittent tenesmus, the birth canal should be examined for the presence of another fetus. Similar symptoms are exhibited by the bitch and queen. In rare instances, in large breeds of dogs, such as the Great Dane, St. Bernard and Newfoundland, the bitch may exhibit every outward sign of having finished whelping. Several days later the bitch may develop anorexia, depression, elevated body temperature, pulse and respiration, and a green, possibly fetid vaginal discharge due to a decomposing fetus. Careful palpation, or preferably a radiograph, of the abdomen after whelping would have avoided leaving a fetus in the atonic uterus.

After every dystocia operation the genital canal, including the uterus, should be examined for the presence of an invaginated uterine horn, lacerations, or ruptures. Small superficial tears of the cervix, vagina, or vulva are of little importance or significance unless retention of the placenta favors infection. In the region of the vulvo-vaginal border these lacerations may lead to infection

*Holmes Symphysiotomy Chisel, Holmes Serum Co., Inc., 1301 Knotts Ave., Springfield, Ill. 62703.

and necrosis with secondary swelling, pain, and tenesmus. Parenteral antibiotic therapy and local treatment with healing protective ointments are indicated. Lacerations of the cervix if extensive may lead to cervical induration and chronic cervicitis. Any tears in, or ruptures of, the uterus should be noted, inasmuch as the prognosis in these latter cases is poor. In large tears in the vulva, vagina, cervix, or uterus, suturing might be attempted by working through the birth canal. Pulling the cervix and uterus back to or outside the vulva, if possible, would make suturing easier. A small uterine rupture especially of the dorsal wall of the uterus may heal spontaneously; but the uterus should be stimulated to contract by the use of oxytocin. Antibiotic therapy and letting the genital tract strictly alone may save a few cases. In extensive ruptures of the uterus, especially where infection exists, slaughter is advised. In less severe cases laparotomy and hysterectomy or suturing of the uterine tear may be indicated.

The placenta and placentomes should be examined in cows and mares. If the placentomes are firm and hard, retention of the membranes generally follows. If uterine infection is obviously present, preventive steps may be taken to control infection by parenteral antibiotic therapy, local treatment of the uterus with antiseptics or tetracycline or other antibiotic compounds and possibly oxytocin to stimulate uterine involution and prevent uterine sepsis. In the bitch if placentas are still present in the uterus they may be withdrawn by the use of a gauze sponge on a forcep. Twisting the instrument in the uterus may catch and hold the placenta to be withdrawn. If retained placenta is suspected the owner should be instructed about subsequent aftercare of the case.

In most obstetrical cases involving forced extraction or fetotomy a dose of 3 to 5 ml., 30 to 50 units, of oxytocin in large animals; 1 to 3 ml., 10 to 30 units, in ewes, does and sows; and 1/2 to 1 ml., 5 to 10 units, in bitches and queens is indicated to prevent possible prolapse of the uterus and aid involution of the uterus and dropping away of the fetal membranes.

If the animal is unable to rise, further examination should be made to determine whether obturator paralysis, dislocation of the hips, pelvic, or spinal injuries are present, and if so the degree of severity. Hypocalcemia in the cow may be masked by the dystocia. Occasionally the administration of oxytocin without a concurrent injection of a calcium product may precipitate milk fever or hypocalcemia in a dairy cow. The cow's udder should be examined to make certain no pathology is present, or that teat wounds and lacerations did not occur during the dystocia.

If the operator has been working with his bare arms in an infected uterus he should wash his arms and hands

very carefully and thoroughly with soap and water and apply an antiseptic in order to prevent skin infections. If any infectious material has adhered to his clothes they should be changed before he goes to another farm. Boots and equipment should be washed and disinfected.

Cesarean Section

Cesarean section is the delivery of the fetus, usually at parturition, by laparohysterotomy. This operation is performed when mutation, forced extraction, and fetotomy are deemed inadequate or too difficult to be employed to relieve the impending or present dystocia or when it is desired that the fetus be delivered alive. The word cesarean is said to derive either from an edict by Julius Caesar that women about to die in advanced childbirth should have this operation performed to save the child, or from the Latin *caeso matris utera*, cutting of the mother's uterus. It is a misconception that Julius Caesar was born in this fashion, as his mother survived his birth in an era when this was impossible.²¹

John Field in 1839 was the first to report this operation in the English literature.⁵⁷ He operated on two bitches. The next year J. B. Carlisle reported on a cesarean section in a sow. Cesarean operations on cows, mares, sows, and bitches were reported soon after. Later, with the advent of anesthesia, suturing techniques, aseptic techniques, and antibiotic therapy, this operation became increasingly common. Cesarean section in the domestic animals has been well-described.^{1,2,7,9,38,47-52,53}

Cesarean section in the Mare may be indicated in pelvic fractures with exostosis, transverse dorsal or transverse rotated bicornual pregnancies, anterior longitudinal presentation with the rear limbs extended beneath the body (dog-sitting posture), torsion of the uterus, fetal monsters such as hydrocephalus, and possibly emphysematous fetuses. In rare dystocia cases in mares where mutation, forced extraction or fetotomy procedures do not offer promise of successful delivery, cesarean section should be considered. In one large clinic 15 fetotomies were performed for each cesarean section.⁴⁸⁻⁵⁰ In many instances the equine fetus is dead because the severity of the parturient problem is not recognized early enough, preferably before parturition, and the time from the onset of labor to the death of the fetus from placental separation or other causes is only 30 minutes to a few hours. The prognosis for a successful equine cesarean operation is poor if prolonged attempts at forced extraction or fetotomy precede the decision to operate. With modern surgical techniques, asepsis, anesthetics and antibiotics successful terminations of this operation on mares

are being reported with increasing frequency. It is no longer necessary to sacrifice the life of the dam to save the fetus. A number of cases have been reported in which the mare conceived following the operation.

The first successful equine cesarean was performed in Hungary in 1908.²⁰ Since then many reports and reviews on equine cesarean section have appeared.^{47b} In 1972 one study made a comparison between 129 equine fetotomy and 63 cesarean operations.^{47a} In the fetotomy cases there was a 10 percent mortality rate, 28 percent retention of the placenta and of those mares rebred a pregnancy rate of 42 percent with an abortion rate of 10 percent. In the cesarean cases there was a mortality rate of 20 percent of mares and 70 percent of foals, 50 percent retention of the placenta and of those mares rebred a pregnancy rate of 50 percent with an abortion rate of 30 percent. In 71 equine cesarean operations 82 percent of the mares survived but only 28 percent of the foals as 64 percent were stillborn. Of 27 mares bred after cesarean section, 50 percent became pregnant but 6 of 14 aborted at 7 to 10 months of gestation.^{47b} Thus, if at all feasible, vaginal delivery in mares is preferable to cesarean section.

General anesthesia is indicated when the fetus is dead. This usually consists of epidural anesthesia and tranquilizers prior to induction by a 5 to 10 percent glycerylguaiacolate in a 5 percent glucose solution to which an ultra-short acting barbiturate such as thiamyl sodium may be added. This is given intravenously to effect. In modern clinics halothane inhalation anesthesia may be used. These general anesthetics may have an adverse affect on the fetus if it is alive. Tranquilizers and local anesthetics in the form of epidural analgesia and local blocks of the abdominal area, or infiltration of the incision sites have been used when the fetus is alive. One clinic recommends using epidural anesthesia, glyceryl guaiacolate and local infiltration anesthesia.⁴⁷ The mare should be restrained in a recumbent position on the left or right side or back depending on the site of the incision.

Various incision sites have been successfully used in the mare and the site should be determined on the basis of the nature of the dystocia, and the presentation or position of the fetus particularly the location of the head of the fetus. The most popular incision site is the Marcenac approach in the left flank starting at the middle of the last rib and extending caudal and ventrally toward the stifle. The incision is usually 25 to 40 cm. in length.⁴⁷ Other reported incision sites have been in the upper left flank or the left paramedian or midline abdominal areas.^{2,53} Herniation is less common with the flank incision sites. Operations in the right flank area are complicated by the large cecum and its dorsal attachments. When incising

the peritoneum care should be taken not to injure the viscera.

The equine uterus is more difficult to bring to the incision than is the uterus in cattle, but if the proper incision site, the Marcenac site in the lower left flank is probably the best, has been selected this can probably be done. Excessive manipulation of the viscera or contents of the abdominal cavity should be avoided as this may precipitate shock symptoms and death. If the uterus is infected great care should be used to avoid contamination of the abdominal cavity. The incision of the uterus should be on its greater curvature over a fetal prominence. Because of the long fetal extremities, mutation, forced extraction and even partial fetotomy may be necessary to remove the fetus. If the foal is alive when delivered the umbilical cord should be left intact for a few minutes until respirations have been established. If the placenta comes away easily it should be removed, otherwise the uterus should be promptly sutured.

A complication of the equine cesarean operation is the rather diffuse bleeding that occurs from the submucosal area of the uterus after it is incised. To prevent severe intrauterine bleeding a continuous lock stitch suture of catgut should be placed through the endometrium, submucosa and serosa completely around the uterine incision for a depth of 1 cm being careful not to include the placenta. This suture was inverted into the uterine cavity by a double row of Lembert or Cushing sutures used to close the uterus after the fetus had been removed.^{47,53} The peritoneum, muscle and fascial layers of the abdominal wall should be sutured separately with #2 Dexon or strong #4 chromic catgut to obliterate dead space and subsequent seroma development. The modified Mayo or overlapping mattress suture for closure of the wound on the ventral abdomen was recommended.²⁸ The skin incision was closed with a nonabsorbable nylon suture. They also recommended the use of quill sutures. The use of a tightfitting canvas or elastic support bandage may be indicated.⁴⁰ Severe edema of the incision area with occasional rupture and gaping of the skin wound are not unusual following surgery in the horse.

Aftercare should include stall confinement, feeding limited amounts of laxative feed, administering tetanus antitoxin, oxytocin and broad range antibiotics both locally and systemically. The latter should be continued for 7 to 10 days. Retained placenta was a common problem in equine cesarean operations.^{46,47} To correct this condition 40 units of oxytocin in 1/2 to 1 liter of saline was administered by a slow intravenous drip method over a period of 1 to 2 hours to produce more normal physiologic contraction of the uterus. Colic was avoided, and the afterbirth dropped away promptly in about 80 percent

of the cases. Complications occurring in the postoperative period are shock that occurs within a few hours after the operation due to manipulation of the uterus and viscera, peritonitis that may cause illness and death 2 to 5 days later, and fatal colic due to strangulation of the gut that may develop one to three weeks or more after the operation due to fibrinous adhesive peritoneal bands secondary to a non-fatal peritonitis.²² Four to 5 days after the operation a rectal examination may be performed to break down any adhesions forming around the involuting uterus.⁴⁷ Hysterectomy, as in the cow, is extremely difficult to perform.²⁸

Cesarean Section in the Cow has been performed in increasing numbers by practitioners in the United States since 1940. Prior to that period it was performed only sporadically. Since 1942 the clinic at Kansas State College has performed between 50 to 100 cesareans each year.^{12,13,31,32} Many more cesareans are performed in the western range states, where immature beef heifers are bred on pasture, than in the northeastern dairy states, where bulls are closely confined and artificial insemination is widely used.

Indications for cesarean section in the cow are as follows.^{2,7,30,42} In the United States immaturity and growth retardation or stunting of heifers resulting in fetopelvic disproportion are by far the most common causes. It is seen particularly in beef cattle when the bull runs on pasture with heifer calves. Some young cattle come into estrum and conceive at 4 to 15 months of age with pregnancy resulting in a severe dystocia due to a very small pelvis and genital tract. In these cases the difference between the size of the fetus and the birth canal is marked. Performing fetotomy operations through such a narrow birth canal is very difficult and the fetus is always lost.

Incomplete dilation or relaxation of the cervix may be associated with secondary uterine inertia with advanced involution of the cervix and uterus secondary to torsion of the uterus, or fetal dystocia and emphysema in which the onset of parturition was not observed, or the cow was neglected for 36 to 48 hours. In other cases it may be observed, without a known predisposing cause, due to a primary uterine inertia, or it may be caused by sclerosis of the cervix. In such cases the fetus may still be alive; oxytocin might be given, and the condition of the cervix observed in 3 to 4 hours or more to make certain that parturition was not in its initial stages.

An abnormally large living fetus may be a cause for cesarean section. Apparently normal healthy fetuses may occasionally be too large for birth without total fetotomy excessive traction or cesarean section. If the forefeet but not the head can enter the pelvic inlet or in posterior presentation if the hips are much too large to enter the

pelvis, cesarean section should be considered, as it is frequently easier, safer, and faster than total fetotomy and in many such cases the delivery of a live calf is possible. These large-sized fetuses are most frequently seen in the large breeds, such as Holstein, Charolais, Simmental, Brown Swiss, Shorthorn, and Herefords. They are usually male. The cause of the dystocia may appear to be a large normal fetus; actually, however, the cause may be an abnormal or relatively small pelvis; or both conditions may be present. In breeds of cattle with muscle hypertrophy or double muscling, affected calves frequently require cesarean section for delivery. In other cases the oversized condition of the fetus may be due to emphysema or to anasarca. In rare cases an excessively large fetal giant may be caused by a greatly prolonged gestation period exceeding 300 days. The prognosis in these latter pathologically oversized fetuses is grave because of the overdistention of the uterus, the uterine inertia, and the high incidence of septic metritis and retained afterbirth following the relief of the dystocia. Other causes for oversized fetuses include fetal monsters such as *Schistosomus reflexus*, general ankyloses, and double monsters. At times, certain of these may be more safely and easily removed by cesarean section than by fetotomy.

Other cases where cesarean section is indicated include: a torsion of the uterus that is difficult or impossible to correct by other means; a juvenile hypoplastic genital tract due to poor growth and development; hydrops amnii and allantois when the life of the dam is imperiled by great distention of the uterus and other methods have failed to relieve the condition; marked stenosis of the vagina in prolonged dystocia in heifers due to perivaginal hemorrhage compressing the genital tract; fetal mummification when ordinary treatments fail, or in heifers or young cows with a 6- to 8-month fetal mummy too large to be expelled through the undilated birth canal; when the dam is unable to rise, is exhausted, debilitated, diseased, or near death; and stenosis of the birth canal due to tumors or extensive scar tissue in the pelvic birth canal. In rare cases in cattle with prolonged dystocia the uterine wall contracts tightly around the emphysematous fetus, producing a contraction or retraction ring dystocia. Since forced extraction may cause rupture of the uterus and fetotomy would be difficult, cesarean section may be indicated. Fracture of the maternal pelvis in cattle is rare and therefore cesarean section due to this cause for dystocia is only seldom indicated.

Prognosis—A review of cesarean operations,^{2,31,34,37b,49,57,58,59} indicates that in cattle that are good surgical risks, and are operated on within 6 to 18 hours after the onset of labor, in cases where the fetus is still

alive or very recently dead and the cow is in good condition physically and has not been damaged by excessive manipulation, injury, or infection of the birth canal or uterus, the mortality rate should be less than 10 percent, and possibly only 5 percent. Under field and actual practice conditions the mortality rate might reach 15 percent.

The mortality rate is about 10 to 30 percent in cases where the cesarean section is performed from 18 to 36 hours after the onset of the second stage of parturition. The fetuses are generally dead and occasionally slightly emphysematous; the cow is in poorer condition for the operation, and the genital tract is usually injured or traumatized. In cases in which dystocia has existed for 36 hours or more, the fetus is emphysematous, the cow is usually in poor physical condition, and the uterus is atonic and infected, the mortality rate may reach 30 to 50 percent or more. In 103 cesarean operations where emphysematous fetuses were removed, the recovery rate was over 80 percent in a college clinic.⁵¹ In 121 bovine cesarean operations, mainly in primipara, 93 percent of the dams survived, 60 to 70 percent of the calves survived but the subsequent pregnancy rate was 52 percent compared to the herd average of 80 percent.³⁴ In 340 cesarean and 80 fetotomy operations; the maternal mortality rate for each series was 5 and 9 percent, retained placenta was 33 and 20 percent and conception rates in cows rebred after the operation were 80 and 73 percent, respectively.⁸ In field cases on ranches the death rate after 117 bovine cesarean sections was 17.9 percent but it was 38.4 percent in cows with purulent decomposition of the fetus while in 412 cases of fetotomy the mortality rate was only 8.4 percent.⁴² In this latter study of nearly 2500 dystocias, 2.6 percent of all dystocias terminated in maternal deaths and of these 44.5 percent were slaughtered after the initial diagnosis was made or after unsuccessful treatment was attempted. The decision therefore as to which procedure to use should be based on a careful evaluation of each case.

The more common causes of maternal death are: shock, secondary to exhaustion; toxemia; excessive manipulation of the abdominal viscera as in torsion of the uterus, or when abdominal pressure is released rapidly, as in removal of a large fetus or excessive amounts of fluids as in hydrops; septicemia, pyemia, and toxemia secondary to septic metritis; uterine inertia in prolonged dystocia; retained placenta; peritonitis; or severe necrotic vaginitis due to excessive manipulation and injury prior to the cesarean section. Hemorrhage and ventral hernia are occasional causes of death. In rare cases hemorrhage, especially from the stalk of a torn or lacerated caruncle, may occur in atonic uteri. Ventral hernia may be prevented by proper suturing technique and suture

material. Most maternal deaths occur 1 to 8 days after the operation. In recent years improved surgical techniques, asepsis, antibiotics and supportive therapy have greatly improved the prognosis for recovery even in cases offering great surgical risks.

It is generally stated that from 60 to 80 percent of cows having cesarean section should be fertile and conceive subsequently. Failure to conceive may be due to peritoneal adhesions or to severe endometrial damage secondary to septic metritis. Of 48 cows without adhesions after cesarean section 81 percent conceived, while in 47 cows with adhesions only 51 percent conceived.⁸ The incidence of retained placenta following cesarean section is high, between 20 and 35 percent, and the incidence of metritis may vary from 20 to 50 percent. Fifty to 80 percent of recovered cows conceived after the cesarean operation.^{2,7,52} About 80 percent of the cattle operated upon had an abnormal puerperium due to retained placenta, uterine infection and delayed involution of the uterus. Uterine infections should be expected and preventive treatment given. The reason for this high rate of placental retention after cesarean section is not known.

According to the authors cited above, the incidence of live calves produced by cesarean section is from 30 to 60 percent. This varies with the promptness with which dystocia is observed, the veterinarian summoned, and the operation performed. Fetotomy in cattle with dead fetuses should be carefully considered before performing cesarean section, since cesarean section requires more trained assistance, is more costly, and results in a higher percentage of subsequent sterility. If it appears that a fetotomy is going to be difficult, prolonged, or dangerous to the dam or operator especially in cases in which the birth canal is small or the birth canal is swollen, compressed, or dry making it difficult to perform a fetotomy; or in cases in which the fetus is emphysematous cesarean section should be considered. It should give promise of being a safer, easier means for relieving the dystocia than does fetotomy or forced extraction. Fewer than 1 percent of the dystocias cannot be relieved by cesarean, while 3 to 5 percent will end in failure if fetotomy is employed.⁴⁹

Selection of the Operative Site, Means of Restraint, and Anesthesia—These will and should vary depending upon the case. The operation has been performed in the upper left and right flank, with the animal standing. This site makes the operation easier for the veterinarian as he can perform it standing; the incision can be smaller because the muscle tissues can stretch into a circular shape when the fetus is removed; subsequent herniation is less likely, and many veterinarians are experienced in operating in the flank site because of frequently having per-

formed rumenotomies. The upper right flank approach may be desired when torsion of the uterus is present, as the standing position is of assistance in correcting the torsion. The disadvantages of the right flank incision are that the cow may be more difficult to restrain and control. It is difficult to bring the uterus to the incision, and abdominal contamination with the uterine contents is nearly unavoidable. This is of no consequence when the fetus is alive and little or no infection is present in the uterus; but it is a major disadvantage with a dead fetus and an infected uterus. If during the operation the incision is extended too far ventrally it is difficult to hold the small intestines within the abdomen. If the cow strains, coughs, or struggles intestines may be expelled through the laparotomy incision.

The operation may be performed in the left flank, at which site intestines usually are not present to offer a problem. The operation can be performed more ventrally on this side if it is desired, but the same advantages and disadvantages apply as for the right flank incision. A large full rumen may make it quite difficult to bring the uterus from the right side of the abdominal cavity to the left. Since these upper flank operations are performed with the cow standing, anesthesia consists of a small dose of epidural anesthesia to control straining; a tranquilizer to quiet the animal; local infiltration, an inverted L-block or paravertebral nerve block anesthesia of the flank region.

Some veterinarians prefer to perform the cesarean operation on a recumbent animal by an oblique abdominal incision in the lower left or possibly right flank region below the fold of skin in the flank and above the attachment of the udder on a line between the stifle and the umbilicus, parallel the ventral borders of the ribs. This site allows easy access to the gravid uterine horn. The muscles in this region stretch easily. It is easier to prevent contamination of the abdominal cavity by uterine fluids. There is less possibility that hernia will develop than when the incision is on the ventral aspect of the abdomen. The disadvantage of this site on the right side is that it is necessary to control the small intestines during the operation so that they do not prolapse. In most cases intestinal prolapse may be prevented by making the cow lie on her left side, a position necessary for performing the operation. The lower-left flank as a site for the incision requires the cow to be laid on her right side. On the left side the incision is more caudal than on the right side, and the apex of the uterus can be brought to the incision behind the rumen. Control of the intestines is only occasionally necessary when the incision is on the left side. In these lower-flank incisions the cow is restrained or stretched in lateral recumbency by tying the

two rear legs together and the two front legs together. Anesthesia may consist of an epidural of 40 to 60 cc. of 2 percent procaine or lidocaine solution, which will produce sensory and motor paralysis of the perineum and rear limbs. This will cause the standing animal to stop straining and to go down. If the cow is laying on her side when epidural anesthesia is administered, sensory loss may be incomplete because the uppermost nerves may not be properly blocked. Paravertebral nerve block or local infiltration of the operative site is usually necessary. In some cases a tranquilizer may be desirable.

Other clinicians prefer the ventral median or paramedian approach, with an incision through the abdominal floor. The site between the linea alba and the right subcutaneous abdominal vein has been recommended.^{12,13,31} Others^{6,46,57} preferred to operate 4 to 10 cm. lateral but parallel to the left subcutaneous abdominal vein. In all ventral abdominal incisions the cow is placed on her back and the incision starts at or slightly lateral to the fore udder and extends forward as far as necessary, usually 24 to 32 cm. In this region the apex or ventral portion of the gravid horn can be brought to and outside of the incision, thereby preventing uterine contents being released into the abdominal cavity. This is a great advantage in cases in which the uterus is infected. The abdominal wall is not as thick in this area as in the flank. There is less muscle tissue and fewer blood vessels, especially in heifers, and the abdominal wall is composed mainly of fibrous connective tissue, the abdominal tunic. The presence of the uterus in the abdominal incision usually keeps the intestines within the abdominal cavity. The main disadvantages to this approach is that the abdominal wall at this site is composed of largely fibrous tissue tunics and will not stretch as does muscle tissue. Thus the incision must be longer than in the flank. If the proper suture material and technique are not employed herniation is more common.

The choice of operative site and mode of anesthesia should fit the amount of help available, the nature of the dystocia requiring cesarean section, the type of cow, the nature of surroundings, the location of the fetus and uterus, and the preference of the operator.^{2,7,30,53} It is desirable to have one skilled assistant to aid the operator, and two lay assistants to control the cow, especially if the cow is in lateral recumbency.

To perform the operation in lateral recumbency the operator should place the animal down by using the rope squeeze method after heavy tranquilization or should administer a large dose of epidural anesthesia, 40 to 60 cc. of 2 percent procaine or lidocaine solution. The cow should not be dropped suddenly, as there may be danger of uterine rupture. Local anesthesia may be used on the

incision site, or if the incision is lateral to the mammary veins an L-block or paravertebral anesthesia is satisfactory. The innervation of the abdominal wall in cattle has been described.² In operations on the ventral abdominal floor the hind limbs should be tied together and the front limbs tied together. They should be stretched apart and sufficient help should be available to roll the cow on her back at certain times during the operation. The cow should not be left on her back for a protracted length of time.

The Operation should conform to all other surgical operations on the abdomen with regard to preparation and draping of the operative site. An approach to asepsis should be attempted. Hemorrhage from the incision should be controlled but in the ventral approach hemorrhage, especially in heifers, is slight. The upper flank operation is performed like the laparotomy incision in a rumenotomy, except that the incision is about 30 cm. long. The author believes that the ventral paramedian approach¹³ and the oblique lower left flank or ventrolateral abdominal approach^{6,1,27,33} are most satisfactory for the majority of cases. The former technique will be described in detail. After the skin is incised the cow should be rolled on her back and the rest of the incision completed. After incising the abdominal tunic the fascia of the transverse abdominal muscle and peritoneum is opened and the incision completed with scissors. In about 7 out of 8 cows the omentum is observed covering the uterus and abdominal viscera. This can be incised, but it is better to pull the omentum cranially as it helps to hold the intestines from the incision. One or both arms are inserted into the abdominal cavity and the fetus is grasped through the uterine wall, and the apex of the uterine horn containing the fetus is pulled into or through the abdominal incision as the cow is returned to lateral recumbency. The gravid uterine horn fills the incision and prevents the escape of the viscera. The uterine horn and fetal membranes are incised longitudinally over the greater curvature, avoiding the cotyledons. Incising of the caruncular stalk may result in persistent hemorrhaging. Chains are applied to the limbs of the fetus and by exerting traction in a ventral and caudal direction the fetus is removed. If necessary the incision in the abdominal wall and uterus should be enlarged to prevent tearing. If the fetus is in posterior presentation the head should be fastened by a snare and the two forefeet secured before the fetus is withdrawn. In rare cases fetotomy may be required on the fetus to assist removal. If uterine torsion is present the direction of torsion should be accurately ascertained before the cow is forced down. This is not so important when the standing cow is operated upon. The torsion should be corrected, if possible, by grasping the fetus through the uterine wall and rotating the uterus.

If this is not easily accomplished, the fetus may be removed before the torsion of the uterus is corrected. In cases in which the uterus is greatly distended due to an emphysematous fetus or hydrops it may be difficult or impossible to draw the apex of the uterus through the incision. If the uterine contents are infected the uterus should be pulled tightly against the abdominal incision and the lips of the incision and the abdominal cavity carefully packed off to avoid contamination when the uterine contents are released. The normal noninfected allantoic and amniotic fluids cause no trouble in the abdominal cavity.

After a live fetus has been removed the fetal membranes are left in the uterus. If the fetus is dead the fetal membranes are removed manually if they drop away readily. Otherwise, they are left within the uterus. Some of the excess fetal membranes may be trimmed away with scissors so that they do not interfere with the suturing of the uterus. Because of the high incidence of uterine infections and retained afterbirths following cesarean section it is advisable to place 1 to 2 grams of tetracycline in the uterine cavity whether or not the fetal membranes are removed. The uterine incision is closed with a double row of Lembert or Cushing sutures of No. 1 or 2 chromic catgut. A long straight intestinal needle should be used. The assistant can greatly facilitate the suturing by holding the edges of the uterine incision together. The cow is then rolled on her back, the uterus replaced, and the omentum pulled caudally over the uterus so that when the abdominal incision is sutured the omentum will lie against it. If torsion was not corrected before the fetus was removed it should be corrected after the uterine closure is completed. The uterus should always be examined for the presence of twins, although these are rarely encountered in conditions requiring a cesarean section.

The ventral abdominal incision may be closed in several ways. Good success using a continuous overlapping mattress suture of heavy nylon (Vetafil), #2 Dexon, or umbilical tape through the abdominal tunic, muscle, and peritoneum was reported.^{2,13,53} This is left in place to prevent eventration or herniation. Interrupted double mattress sutures of No. 4 to 5 chromic catgut with a supplementary continuous suture of doubled catgut along the muscle incision after the peritoneum had been securely closed was recommended.^{46,50} Until this second suture line was used occasional cases of herniation occurred. After its use no cases of herniation developed in 48 consecutive cesareans. In the ventral incisions just described, the tough abdominal tunic provides a firm anchorage for the sutures. The superficial muscles and fascia may be pulled together with catgut. Mattress, inter-

rupted, figure 8, or lock stitches of nylon, silk, linen, or umbilical tape are placed in the skin and underlying fascia or muscle.

The peritoneal and muscle layers in the upper flank incisions are sewn with catgut or if preferred the stronger figure-eight sutures of umbilical tape or nylon through all layers including the skin. The skin sutures are usually removed in 7 to 10 days. This operation generally takes from 30 to 60 minutes to perform if complications are not encountered. Three to 5 ml., 30 to 50 U.S.P. units of posterior pituitary extract or oxytocin is given to stimulate uterine contraction and involution. This should not be given until after the operation, because if given earlier, it may complicate the suturing by contracting the uterus and pulling it away from the abdominal incision.

Postoperative Care—Most cases should receive 3 to 6 million units of penicillin or 1 to 2 grams of the tetracycline compounds parenterally after the operation. This should be repeated daily for 3 to 7 days. The cow should be observed closely for the first 24 hours for evidence of shock especially if large amounts of fluid or a large fetus were removed or if there was much manipulation of the uterus or abdominal contents. If shock develops it should be combatted immediately with intravenous injections of blood, saline, and glucose. In rare cases hypocalcemia, and straining due to vulvar irritation or other causes, may occur, requiring prompt attention. If the calf survives it should receive some colostrum soon after birth. If the afterbirth is retained and metritis develops the condition should be handled conservatively by allowing the afterbirth to drop away by itself. It is dangerous to remove the placenta manually, since little can be gained by the attempt, and much lost by injury to the uterus. The cow should be kept quiet and away from contact with other animals after the operation, in order to avoid possible injury to the operative site. The skin sutures may be removed in 7 to 14 days.

Cesarean Section in the Ewe and Doe—This operation has been performed successfully by many veterinarians in recent years but it requires a careful, aseptic technique oftentimes difficult to achieve under farm conditions.^{2,2} Sixty nine ovine cesarean operations to relieve dystocia with a 77 percent recovery were reported.¹¹ Most deaths were due to infection. For this reason the operation is best performed in a veterinary hospital to which the ewe can be transported easily. The operation is indicated in the ewe when the cervix fails to dilate, "ring-womb," or when the ewe is bred too young or is poorly grown and the birth canal is too small to permit the operator to relieve the dystocia by forced extraction. In rare instances monster fetuses, fetal emphysema, fetuses with a large head, torsion of the uterus, and other conditions

similar to those in the cow may necessitate cesarean section. Prolapse of the vagina is a common cause for the cesarean operation in ewes.⁹ However, this may be treated by the induction of parturition with the corticosteroids.² Another indication for a cesarean is in pregnancy toxemia or ketosis in ewes, in which dead twin fetuses are usually present. Under usual circumstances the severely affected ewe would die before the dead fetuses were aborted despite glucose and cortisone therapy and other supportive treatments. The valuable ewe may be saved by cesarean section. The prognosis should be more guarded than in the cow.

The operation is similar to that in the cow and is performed through the flank, through the ventrolateral abdominal wall, through the ventral abdominal wall between the linea alba and the subcutaneous abdominal vein, or through the midline.¹¹ Tranquilizers and epidural, local, inverted L block, or paravertebral anesthesia can be used. If bicornual twins are present in the uterus an incision should be made in each horn. No. 4 chromic catgut is satisfactory for suturing the abdominal wall.

Aftercare of the ewe is similar to that of the cow. If pregnancy ketosis is present glucose injections, propylene glycol orally and cortisone may help promote appetite and recovery in the convalescent ewe.

Cesarean Section in the Sow—has been performed successfully for many years. The sow is more resistant to infection and peritonitis than is the ewe and cow. Cesarean is indicated in the sow when because of being bred too young or of being poorly grown, the resulting small pelvis and genital canal prevent normal farrowing. The canal is usually too small to permit the introduction of the hand in order to apply traction. Cesarean may be indicated in primary uterine inertia that fails to respond to oxytocin or in secondary uterine inertia in which the second stage of labor has been prolonged and lay or veterinary assistance failed to correct the dystocia. In this latter type of dystocia the genital tract is usually swollen and may occasionally be severely traumatized. Cesarean may be indicated occasionally due to monster fetuses or to pelvic fractures with exostoses or other abnormalities.^{2,9,38}

Cesarean section in the sow is 85 to 90 percent successful when performed soon after the onset of the second stage of parturition, when the fetuses are still alive and the sow or gilt is still strong and vigorous. Mortality in the sow rises when the operation is not performed until 18 to 24 hours after the onset of straining. By this time the pigs are usually dead and the sow is in poorer shape for the operation. If the operation is delayed more than 24 hours the fetuses are usually emphysematous, the uterus infected, and the sow exhausted and toxic.

Although some sows may survive surgery at this stage the prognosis is guarded to poor depending upon the condition of the genital tract.

As in the ewe, the operation should be performed in a veterinary hospital if possible inasmuch as the average hog farm is rather unsanitary and inconvenient for surgery. If it must be performed on the farm the sow's legs and body may be strapped to a panel and the panel placed across two supports, to form a satisfactory operating table set up in a clean, dust-free location. Many veterinarians prefer to use heavy tranquilization and to supplement it with local anesthesia along the incision line. Epidural anesthesia with 2 to 4 percent procaine or 2 percent lidocaine solution injected in 8 to 10 ml amounts into the epidural space at the lumbo-sacral articulation has been recommended.^{13,15,38} The operator should make sure that the sow's foreparts are kept elevated or level, so that the anesthetic solution does not gravitate forward. Surgical preparation and procedures similar to those in the cow and ewe should be carried out in preparing the operative area and maintaining near asepsis during the operation on the sow. For this purpose a large sterile rubber or plastic shroud to drape over the sow's body is very helpful.

A vertical incision, 17 to 20 cm., in length in the upper flank region^{13,38} or a horizontal flank incision parallel to but 1 to 3 inches above the mammae have been recommended.²⁶ A midline abdominal incision site is not recommended for obvious reasons. The large amount of fat between the peritoneum and the body wall may cause some confusion unless it is recognized. One entire horn may be drawn through the incision to the outside before incising and removing the fetuses; or one fetus can be brought to the outside and removed, then the next fetus brought out and removed through the previously-made incision; and so forth until all the fetuses in the one horn have been removed and the horn is completely outside the abdomen. The fetuses may be pulled from the inside of the horn or forced toward the incision by pressure on the outside of the horn or a combination of both in order to facilitate their rapid removal. The pelvic portion of the canal should be examined to be certain a fetus is not left there. If the fetal membranes are expelled with the fetus they are removed. If not expelled with the fetuses they are left in the uterus to be expelled later—usually within 12 hours. The incision is sutured with a single or double row of Lembert or Cushing sutures of No. 1 chronic catgut and that horn replaced. The same technique is followed on the other horn. In exceptional cases, if the uterus is well-involved it may be necessary to incise the horn in several sites. If the uterus is severely infected, introduction of antibiotics—especially the tet-

racycline derivatives—is indicated prior to closure of the uterine incisions. The peritoneum and muscle layers are sutured separately with chromic catgut or Dexon by continuous sutures; and the skin with silk, nylon, Vetafil, or umbilical tape.

For aftercare of the sow administration of oxytocin and antibiotics are indicated, as in the cow. The sow should be confined in a clean, quiet place for 8 to 10 days, at which time the skin sutures may be removed.

Cesarean Section in the Bitch and Queen is very common and useful in the correction of dystocia in these species. It is performed most commonly in primary uterine inertia that fails to respond to "feathering," or vaginal stimulation of uterine contractions, or to the injection of oxytocin. This condition is seen most commonly in certain toy breeds such as the Dachshund. It is frequently required to relieve dystocia in the brachycephalic breeds of dogs with large heads and small pelves, such as the Boston and other bulldogs, Pekinese, Boxers, Pugs, and even the Scotch Terriers and Sealyhams. There is no doubt that cesarean section has been a great boon to these breeds of dogs. The discussion that centers around the fact that this operation has been conducive to the perpetuation of such abnormal breeds is a subject of importance, but is not discussed here because it is not appropriate to this text. Cesarean section may be indicated in Cocker, in which for apparently psychotic reasons whelping does not progress normally. It is indicated when pelvic fractures, tumors, rickets, or the rearing of a young dog under unfavorable conditions has resulted in dystocia due to a small pelvic canal. It is indicated in secondary uterine inertia in which more fetuses are still in the uterus and dystocia has been prolonged so that even if 1 or 2 fetuses could be removed by traction, the rest would not be expelled, because of uterine atony and fatigue. It may be indicated with 1 or 2 excessively large fetuses, or when a fetus is transversely located in the uterine body and cannot be removed manually. In rare instances it may be indicated for uterine torsion and for retention of one fetus in the uterus following apparently normal parturition, as is seen occasionally in the large breeds, such as the Great Dane and St. Bernard. The cesarean operation may also be used to remove mummified fetuses from the uterus and in cases of inguinal hernias containing a portion of the pregnant uterus.² It may be indicated when general debility and inanition make normal parturition impossible. When a greenish-black discharge appears at the vulva it is an indication that the placentas are disengaging, and cesarean might be indicated even though probably one fetus or more are dead.

The same general indications for this operation apply to the queen. In the queen the most common cause for

dystocia is deviation of the fetal head and neck, and if mutation per vaginam is not successful a cesarean operation is indicated.

Many veterinarians perform cesarean operations when possibly mutation or forced extraction could be used because they are surer of their results with this operation. They are better acquainted with it than with the other techniques in which fetuses might be injured by improper or unskilled use of instruments per vaginam. The operation is frequently employed because it requires much less time and patience of the busy practitioner. Otherwise the veterinarian might have to observe and assist the bitch at intervals for 4 to 6 hours or more. Besides this inconvenience to the veterinarian, it would be more costly to the owner. Lastly, many owners, expecting the bitch to be in dystocia because of its breed or past history, request and expect the veterinarian to perform a cesarean operation.

Prognosis—Cesarean section in the bitch when performed during the first stage of labor or within 12 hours after the onset of the second stage of parturition when the fetuses are still alive, should result in less than a 2 to 3 percent mortality rate. In many hospitals this may be less than 1 percent. If the operation is not performed until 12 to 24 hours after the onset of labor some of the fetuses may be dead, but the results nevertheless are usually quite good. If the operation is delayed beyond 24 hours after the onset of labor the maternal mortality rate may be 50 percent or more due to shock, toxemia, septic metritis, and exhaustion. In these neglected cases the fetuses are usually dead, the uterus diseased and atonic, and hysterectomy may be indicated.

In general, bitches should be examined if they have labored for 3 to 4 hours without delivering a fetus. The cause of the dystocia should be determined and if cesarean is decided upon it should not be delayed too long by efforts to remove fetuses by other means. Fetotomy is rarely possible in the bitch or cat due to the small birth canal. In cases in which dystocia, relievable only by cesarean, is expected on the basis of the previous breeding history or examination, the bitch should be observed closely for signs of beginning parturition. Body temperature readings may be made 2 or 3 times daily and when the temperature drops 1 degree or more below normal or goes below 100° F. the bitch is either in the first stage of labor or beginning the second, and a cesarean operation should be performed immediately. Cesarean section apparently has little effect on the subsequent fertility of the bitch; many bitches have had from 4 to 8 cesarean operations performed without becoming sterile, even though slight to severe adhesions may form at the operative site. After 3 cesarean operations adhesions are

common and the number of pups per litter decrease and operations are more difficult to perform.¹

The Operation should be performed in a skillful, aseptic manner under hospital or clinic conditions. Complications should be anticipated and prevented or handled. Extra aid should be present for receiving the pups as they are delivered. An incubator that provides warmth, 85 to 90° F, and oxygen may save many pups.²³ Pre-medication for the canine cesarean operation consists of a small dose of atropine. After the operative site has been prepared an ultra short acting barbiturate is administered followed by a light plane of halothane or methoxyflurane or ether anesthesia. **Innovar**, a neuroleptanalgesic has been used and followed by naloxone to reverse its action in the bitch and pups after the operation. Local anesthesia may be used in the bitch in either of the above procedures to reduce exposure to the anesthetic. **Doxapram**, a respiratory stimulant, may aid recover of the pups. In the queen the above anesthetics may be used with the exception of **Innovar**. If local anesthesia is used in the queen diluting 2 percent lidocaine to 0.5 percent is indicated to avoid overdosing.⁴¹ In the queen a combination of zylazine and **Ketamine** have also been used but since these drugs also affect the intrauterine live fetuses, delayed recovery after birth is to be expected. Epidural analgesia is the method preferred in the bitch by some veterinarians.²⁴

The incision may be made through the flank at an oblique angle parallel the last ribs. This site reduces the possibility of eventration but may leave a noticeable scar in shorthaired dogs. The approach takes more time, the horns are harder to reach, and an incision must be made in each horn. A left-flank incision 7 to 12 cm long parallel to the spine and beginning 3 cm. behind the costal arch and 3 cm above the mammary glands provided better access to the uterus, and the scar is less noticeable.⁴ Many other veterinarians prefer the midline, or linea alba, as an incision site. The greatest disadvantages to this site, which are not serious, are possible eventration or injury to the wound by the pups. It has the advantage of easy access to the uterus. Because the withdrawal of the gravid uterus through the incision might predispose to shock, pressure should be applied to the abdomen after removal of the gravid uterus, and then gradually released. To prevent shock some veterinarians bring the uterus and a fetus to the incision, pack the incision with towels and incise each horn, removing the fetuses by pressure and traction, and keeping the uterus within the abdominal cavity. Because this procedure might result in peritonitis from uterine fluids, it is not desirable unless the fetuses are alive and the uterus not infected. This technique is also more time-consuming. Most veterinarians remove

one horn of the uterus at a time through the abdominal incision. The horn is incised near the bifurcation. The fetuses may be removed from one or even both horns through the same hysterotomy incision. The uterus is incised longitudinally on the side opposite the attachment of the broad ligament, care being exercised not to incise through a placental area. After the fetus is removed the placenta will come away by pressure on the outside of the uterine horn over the placental area of attachment. This can be aided by tension on the umbilical cord. As the fetuses are removed the umbilical cord is clamped with forceps which should not be allowed to dangle as this might predispose to hernia. The placenta is cut or torn away.

The pups are rubbed with a towel to stimulate respirations. The pup's head is held down, to facilitate drainage of mucus from the nostrils and throat. If respirations are delayed, the pup should be dipped alternately into hot and cold water, or its umbilical vein injected with a respiratory stimulant like **Doxapram**. This may also be placed under the tongue and absorbed there.^{41,55} The pups should be kept warm, 80° F. or higher, until placed with the bitch for nursing. Each horn should be carefully checked to be sure all fetuses are removed. If a fetus should be in the birth canal it should be removed by traction through the vagina or drawn cranially through the incision in the uterine body.

The uterine incision is closed by a single or double row of Lembert sutures of catgut. The flank incisions are sutured with several rows of catgut or Dexon with nylon or silk in the skin. The peritoneum on the midline incision is sutured with continuous catgut, the fascia of the linea alba with nylon, and the skin with interrupted nylon or silk sutures. The skin wounds are covered with adhesive if surgery was aseptic. If the wound is likely to be infected it should be left open for daily dressing and bandaging. Gauze or other dressing may be wrapped around the body between the breasts, but not so tightly as to cause discomfort. This is difficult to hold in place. After the operation all pups, especially those of the brachycephalic breeds, should be checked for abnormalities such as cleft palate, hydrocephalus, and so forth, and deformed pups destroyed.

Aftercare of Bitch and Pups—After the bitch has recovered from the anesthesia the pups are placed with her. If she does not encourage their suckling or ignores them she should be restrained or tranquilized while they suckle for the first several days until she “adopts” them. If the bitch should succumb, orphan pups may be raised on rich cow's milk or goat's milk, 1 to 5 parts of evaporated milk and water, or “Esbilac” (Borden's). A formula for feeding pups of 8 ounces of homogenized milk

containing 2 egg yolks may also be used. About 1/2 to 3/4 oz. is given every 8 hours for the first week or two and by the third and fourth week about one ounce, 80 to 100 calories per lb. of body weight, is given every 8 hours.^{2b,39} Pups should be dried after they are fed. Defecation in the pups will be stimulated after they have eaten by their being rubbed beneath the tail with cotton dipped in olive oil. In a week or so some pabulum may be given. Later they can be fed milk from a dish or pan. Ground meat, cereal and ordinary cow's milk can be given when they are 3 weeks of age. Pups can be completely weaned at 4 to 5 weeks after birth.

The aftercare of the bitch following cesarean operation is similar to that given the cow, in that a small dose of oxytocin 1/2 to 1 cc., 5 to 20 units, or ergonamine is given to aid contraction of the uterus. The bitch should be placed on parenteral antibiotics for several days or more and observed closely for symptoms of shock, peritonitis or sepsis the first 6 to 48 hours. If this is suspected or occurs, prompt administration of blood and saline is indicated, along with keeping the bitch warm. The abdominal wound should be observed for any evidence of infection or breakdown or evidence that the incision has been licked or chewed. If it has, muzzling or other restraint of the bitch may be necessary. If the fetuses are dead, the size and congestion of the mammary glands may be reduced by massaging them with camphorated oil. It is advisable to send the bitch home, where she will be in a familiar environment, as soon as possible after the operation. The stitches may be removed about the seventh day after the operation.

Hysterectomy

Occasionally hysterectomy may be indicated due to prolonged dystocia, in which much trauma, injury, and even rupture of the uterus has been produced by unsuccessful fetotomy, mutation, or forced extraction operations, or the fetus is emphysematous and the uterus is atonic, severely infected and diseased.² In severe uterine torsion in which the uterine circulation is obviously compromised hysterectomy is indicated. The dam is usually toxic and exhausted, with a subnormal temperature, anorexia, and a rapid, weak pulse. It may be obvious before the operation or at least at the time of the laparotomy that cesarean section alone, without hysterectomy, will not save the life of the dam. In cases where there is a severely diseased uterus, hysterectomy offers the only hope of saving the dam. The prognosis is always very guarded to poor, since shock and peritonitis generally cause death in these already poor operative risks. In cases

such as severe rupture or laceration of the uterus during fetotomy or forced extraction, hysterectomy might occasionally be considered.

In mares, cows, ewes and sows hysterectomy is usually of questionable value as the economic value of the animal does not generally warrant the expense and effort of surgery and aftercare because the mortality is high. Because of the large size of the uterus and fetus or fetuses it may be necessary to remove the fetuses first in order to remove the uterus. Contamination of the abdominal cavity is difficult to avoid when tying the uterine and ovarian arteries and removing the uterus. After removal of the uterus, eversion of the cervix or uterine or vaginal stump offers further severe difficulties. Shock frequently develops. Successful hysterectomy has been reported only occasionally in cows and sows and rarely in mares.²⁸

In bitches and queens hysterectomy is more often successfully employed because working conditions are good and the animals and their uterus and fetuses are relatively small.² Hysterectomy is often considered in bitches and queens with a prolonged dystocia of 24 to 36 hours or more.² In 52 cesareans and 52 hysterectomies the recovery rate was 82 percent and 67 percent, respectively. The recovery rate was only 50 percent when the fetuses were putrid.²⁹ The prognosis in cases in which hysterectomy is necessary in bitches and queens is therefore guarded. Prior to and during surgery, proper attention should be paid to preventing shock and the contamination of the abdominal cavity. A plentiful supply of instruments should be available. Because the animal is a poor surgical risk anesthesia should be selected and used carefully. A relatively small dose of a tranquilizer with local anesthesia of the incision site is often used in these cases. A midline incision is favored in a hysterectomy operation. If possible the fetuses should be removed within the intact uterus to avoid contamination of the abdominal cavity or incision. Care must be used in exteriorizing the uterus so that tearing of a vessel and subsequent hemorrhage does not occur. Double ligatures should be fastened securely around the utero-ovarian, uterine and caudal uterine arteries. At times excessive fat complicates the placing of tight ligatures around the large vessels in the broad ligament. Forceps are placed across the body and cervix of the uterus after the broad ligament has been incised and the ovaries and uterus are free. The uterus, fetuses, and ovaries may be removed by incising the body of the uterus between the forceps. The serosa of the stump of the uterus should be inverted by a Parker-Kerr stitch as the forceps are removed. After surgery the bitch should be kept warm and given blood and fluids to prevent the shock that sometimes follows the removal of such a large

organ. Antibiotics and corticosteroids should be administered to control possible abdominal contamination and necrosis of the liver associated with shock. Careful continuous aftercare and nursing of these cases should be given.

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Chapter X

DIAGNOSIS AND TREATMENT OF VARIOUS TYPES OF DYSTOCIA

In previous chapters the causes, equipment, and operations for the handling of dystocia were outlined. In this chapter the various conditions which produce dystocia and the practical handling of these problems will be discussed under the headings of: dystocia due to pathological presentation, position, and posture of the fetus; abnormal size of the fetus; postmortem changes in the fetus; uterine displacements; stenosis of the birth canal; and uterine inertia.

Dystocia Due to Pathological Presentation, Position, and Posture of the Fetus

Pathological presentations, positions, and postures are apparently due to a combination of uterine inertia and a reduced viability and activity in the fetus especially during the first and second stages of parturition. Uterine inertia may be caused by hormonal or disease factors causing a lack of, weak or irregular contractions of the uterine wall. If the fetus is diseased, deformed, lacks vigor, or is dead, its movements and righting reflexes are weak or absent, and postural abnormalities in such cases are common. In the mare, bitch, and sow these factors when combined with a normal dorso-ilial or dorso-pubic position prior to parturition may result in the failure of the fetus to rotate into a normal dorso-sacral position at parturition. As the fetus is forced through the birth canal the catching or impinging of an extremity at the pelvic inlet causes a progressive flexing of that extremity as the remainder of the fetus passes beyond it. Transverse pregnancies caused by uterine disease, abnormal attachment and development of the fetus and its membranes, or in the case of multipara a single fetus developing in both horns transversely across the body, usually result in dystocia. (See Figures 86, 89, 90.)

Dystocia in Anterior Presentation may result from the following types of abnormalities:

Dorso-ilial or Dorso-pubic Positions are observed in all species as a cause of dystocia, especially in unipara, particularly when the fetus is of normal or large size. In rare cases small or premature fetuses are expelled in these abnormal positions. In these dystocias the fetus should

be rotated into a normal dorso-sacral position before being removed. (See Figure 90.) Before doing this, one should carefully observe and examine the uterus and genital canal to make certain that torsion of the uterus is not the cause of the abnormal fetal position. If torsion is present the fetus should be rotated in the direction which will reduce the torsion. Many of the fetuses found in this position are weak or dead. Lubrication of a dry birth canal prior to rotation of the fetus is of great assistance.

Deviations of the Head and Neck are common types of abnormal posture in anterior presentation causing dystocia in all species. In swine, because the neck is so short, this type of dystocia is very rare. The deviation of the head and neck may be in any direction. Lateral deviation of the head is seen most often in unipara. The deviation may be directly lateral, with the head alongside the thorax in the bovine fetus, or alongside the flank of the equine fetus. This lateral deviation may also be obliquely upward or downward, and occasionally the head may be rotated 45 to 90 degrees on the neck. Diagnosis in the cow is easily made by finding the two forelimbs in the birth canal, but not the head. By passing the hand and arm as far alongside the fetal body as possible and then carrying it around the body, the head and neck are found and the direction of the deviation noted. In the mare this may be more difficult because the head is usually out of reach of the hand. By locating the withers and mane or the trachea of the equine fetus these may be followed to the left, right, downward or upward and the direction of the deviation determined. If the bovine fetus is alive and labor has not been in progress more than 4 to 12 hours the deviation may be corrected with the least amount of difficulty by means of mutation. This is best performed under epidural anesthesia with the animal standing. If the animal is down it should be placed in lateral recumbency with the rear parts higher than the foreparts and with the fetal head in the upper flank of the dam, above the fetal body. Repulsion on the fetal chest in an oblique manner is performed. The body of the fetus is pushed away from the fetal head and neck so that room is produced to allow correction by traction on the fetal head. The incisor teeth should be guarded to prevent laceration of the uterus. If the dam is recum-

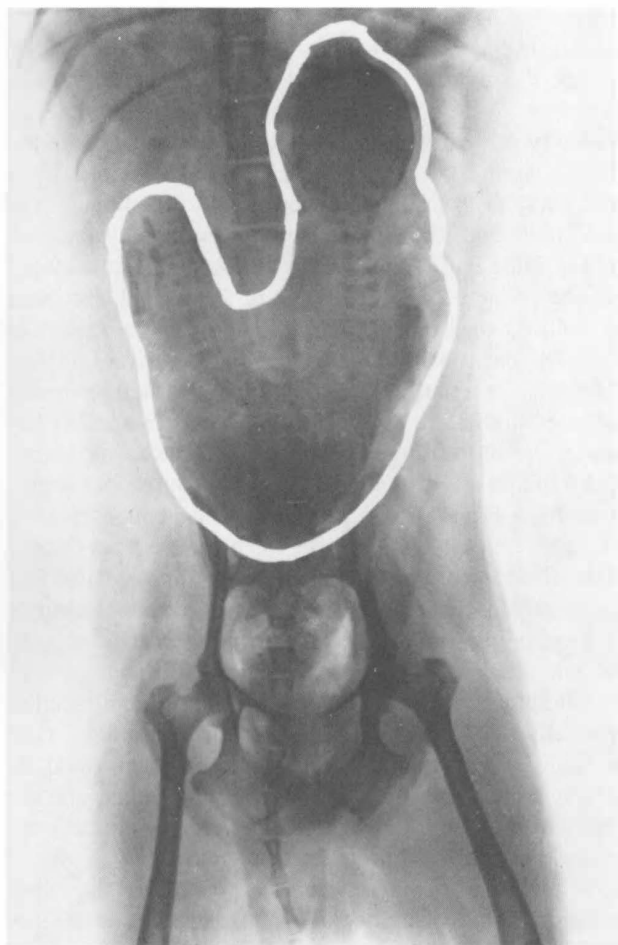


Figure 89. Dystocia due to a transverse presentation of a single fetus in a Pomeranian bitch. This was relieved by a Cesarean operation.

bent it is helpful, particularly in the mare under general anesthesia, to have an assistant exert caudal pressure on the fetal head through the mare's flank, helping to force it back toward the operator's hand. In the mare caudal traction on a loop of chain passed around the neck or the use of a detorsion rod to push the chain loop toward the head before applying traction may aid in bringing the fetal head near enough the pelvis to grasp with the hand, hook or snare and thus correct the deviated posture. If the neck and head are twisted this is corrected in the uterus by grasping the muzzle or the orbits with fingers and rotating the head in the proper direction as traction is applied to the jaw, drawing the head and the forelimbs into the birth canal. In the bitch and queen lateral deviation is corrected by vaginal manipulation with the finger, and pressure applied through the abdominal wall. Forced extraction should never be applied to these cases

of deviation of the fetal head and neck without first correcting the abnormal posture. If mutation fails because the fetus is emphysematous or because the uterine wall is contracted tightly around the fetus, fetotomy and amputation of the head and neck with the fetotome is indicated. Occasionally it may be necessary to amputate the opposite forelimb at the elbow joint or to remove the entire limb in order to move the fetus nearer the vulva so that the wire can be placed around its neck. In the bitch and queen cesarean section or in exceptional cases hysterectomy may be indicated.

Wry-neck is seen occasionally in equine and bovine fetuses. It usually occurs in transverse bicornual pregnancy in the mare in which movement of the fetal head and neck is restricted or prevented during most of the gestation period. It may occur in a longitudinal pregnancy with the fetus in one horn and the body. The outer bones of the face become convex while the facial bones lying against the fetus are concave, due to the pressure applied by the uterine wall. The cervical vertebrae are curved and the articulations and atrophied muscles produce a sharply-bent "muscle contracture" condition of the neck resembling torticollis that cannot be straightened, even outside the dam, without fracturing the cervical vertebrae. A bicornual or transverse pregnancy with a wry-necked fetus may rarely at the time of parturition undergo spontaneous version into an anterior or posterior presentation.⁴² In posterior presentation dystocia seldom if ever occurs. The extreme bend in the neck, the stiff, firm neck, and the fact that the head and neck move with the fetal body and cannot be straightened, aids in confirming the diagnosis. Fetotomy is indicated and amputation of the head and neck is simple and practical



Figure 90. Normal dorso-pubic position of an equine fetus late in gestation. The fetus must rotate into a dorso-sacral position during the early stages of parturition or a dystocia will result.

with the fetotome. Removal could also be effected by the removal of the opposite forelimb and evisceration. With forced extraction the fetus could then be withdrawn with the head occupying the space of the removed viscera.

Downward deviation of the head between the forelimbs is occasionally seen in all species except swine. In mild cases, only the nose of the fetus is caught on the brim of the pelvis with the forehead entering the pelvic inlet, "vertex presentation." In more severe flexing of the head and neck the ears and the top of the head are presenting, "poll presentation." This is usually corrected by mutation by repelling the fetus and grasping the muzzle of the fetus and raising it into the pelvic cavity. In the more severe cases the neck extends between the forelimbs, "nape presentation," and the head is against the fetal sternum or abdomen. This latter condition is more difficult to diagnose but by means of careful palpation the operator will notice that the forelimbs do not come together, and that in the mare the mane of the fetus may be felt between the legs, and the head found beneath the fetal body. In cases which are diagnosed early, mutation may correct the deviation. As an aid in relieving this type of dystocia, after the fetus is repelled a forelimb may be flexed alongside the body and the abnormal posture of the head and neck corrected by moving them laterally beneath this leg. The abnormal position of the limb is then corrected and the fetus removed by traction. In the mare, or in bovine cases diagnosed after prolonged dystocia, fetotomy is necessary. Removal of one forelimb and then correction of the deviation by mutation has been recommended.⁴² It may be advisable to amputate the head and neck and one forelimb by a single cut with the fetotome when the fetus is emphysematous or the uterus strongly contracted. In some cases cesarean section may be indicated in the bitch and queen. Upward deviation of the head is rare in the cow and mare but occasionally it is found as a cause for dystocia in bitches and queens. The handling is the same as in lateral deviation of the head and neck.

Deviations of the Forelimbs are relatively common causes for dystocia in uniparous animals. They are rarely a cause for dystocia in multipara because their forelimbs are short and flexible. In unipara, especially the cow and mare, normal birth cannot occur, unless the fetus is very small or premature, with one forelimb extended or retained alongside the body. Forced extraction should not be attempted. In ewes normal birth can occur with one forelimb retained. If dystocia is present with this posture and the ovine fetus is not too large, dystocia may be relieved by forced extraction without mutation. During birth the shoulder and large shoulder joint are displaced

forward alongside the neck when the forelimb is extended in the normal manner. This is made possible by a lack of a clavicle in these species. Pathologically when a portion of the forelimb is caught at the pelvic inlet or in the birth canal the leg is forced backwards toward the body, flexing the shoulder and the elbow joints. Dystocia results from the shoulder being pushed back over the chest, and thereby increasing the pectoral diameter of the fetus. In mild, early dystocia the toe may be caught on the pelvic brim or by a fold in the genital tract, and the fetlock then becomes flexed. The head is present in the birth canal or at the vulva, with one or no forefeet. Mutation by repulsion of the fetus and traction on the retained limb corrects the dystocia. The fetal toe or claw should be cupped in the operator's hand or handled carefully so that a fold of uterus or birth canal is not caught, causing a laceration or rupture of the genital tract. A more severe dystocia is present when the knees are flexed, knee-flexed posture, or the forelimbs are extended beneath the fetal body. In these cases if the fetal head is not extending through the birth canal the condition may be corrected by mutation. The fetus is repelled under epidural anesthesia. The knees are grasped and repelled cranially and laterally into the cow's flank as the feet are extended medially and caudally into the birth canal. If possible the body of the fetus should be repelled into the flank of the dam opposite the side where the abnormal posture of the forelimb is being corrected.

In dystocia cases when the head is outside the vulva repulsion is very difficult or impossible unless the fetus is small, because the head rapidly becomes very edematous. Decapitation should be performed especially if the fetus is dead or emphysematous. Following decapitation the fetus is repelled and the abnormal posture of the forelimbs corrected. If the forelimb is extended beneath the body traction on the forearm and repulsion of the body cranially and dorsally will bring the leg to a knee-flexed posture. In a very few cases it may be necessary when the fetus is emphysematous and the uterine wall closely invests the fetus to remove the forelimb extended beneath the body by a fetotomy operation. Once the legs have been brought into the birth canal they should be extended by traction and the fetus removed by traction on them and on the head or stump of the neck vertebrae if decapitation has been performed. In rare cases to avoid fetotomy a small bovine fetus may be withdrawn with one leg retained, when the head is outside the vulva and the thorax is in the pelvic cavity.

Dystocia due to the one or both forelegs being crossed over the neck is rare except in the mare. This abnormal posture increases the chest diameters as the elbows are forced against the pubis. It may also result in the dor-

sally-directed hooves engaging the roof of the vagina and causing rupture of the vagina, rectum, or perineum. This condition is readily diagnosed. Traction by the operator's hand or with a snare or chain by an assistant should be placed on the uppermost pastern or foot, if both legs are crossed over the neck, and this leg should be pulled upward and then laterally and downward and medially so the leg is brought beneath the neck and head and fully extended. Elevation of the head helps in placing the legs beneath the head. Repulsion and epidural anesthesia usually are not necessary unless the foot is engaged in the dorsal vaginal wall.

Flexion of the anterior limbs at the elbow is a relatively common cause for dystocia particularly in young cattle. It is caused by the olecranon catching on the brim of the pelvis with the leg not fully extended as the fetus passes into the birth canal. In many instances both elbows are impacted. The elbow and shoulder joints are flexed, greatly increasing the pectoral diameters of the fetus. This condition is diagnosed by the fact that the nose of the fetus is resting on or below the fetlock joints while in the normal extended position the nose rests on the middle of the metacarpal bone. By feeling along the fetal leg the operator finds the olecranon firmly wedged against the pelvic brim. This condition is easily corrected by traction first on one limb and then on the other; or the operator can place his hand under the olecranon and raise it as traction is applied to the limb extending it into its proper posture.

Interlocking of the Maternal and Fetal Pelves or "Hip lock" in Anterior Presentation is commonly observed as a cause for dystocia in heifers. The major trochanters of the fetal femurs are the structures that fail to pass through the bony pelvis of the dam. The tuber coxae in calves are small and rarely if ever are the cause of dystocia. Dystocia due to hip lock may be caused by an improper direction of traction putting tension on the linea alba and increasing the pelvic diameter of the fetus and by traction causing the maternal pelvis to tip caudally and dorsally, thereby reducing the diameter of the pelvic inlet of the dam. In most of the naturally occurring longstanding cases of interlocking of the maternal and fetal pelves, obturator paralysis is observed and always should be looked for before relieving the dystocia. This type of dystocia is easily diagnosed by the fact that the head, forelimbs, and a portion of the thorax extend through the vulva. In dystocia due to fetal ascites, or the hind limbs extending alongside the body or against the pelvis as in the *Perosomus elumbis* monster, the thorax seldom extends through the vulva. There should be a careful examination of the relative sizes of the maternal and fetal pelves. If traction is decided upon, the fetus

and birth canal should be well-lubricated. Traction should be applied by assistants or by the fetal extractor, pulling the fetus in an arc-like curve, first backward and then downward and if the dam is down even exerting leverage with the handle of the extractor between the rear legs. In other cases lateral traction around the dam's hips may aid by pulling the fetal pelvis through the maternal pelvis at an oblique angle or in a dorso-ilial position. Some veterinarians rotate the fetus by placing the arms between the fetal legs and over the neck as gradual traction is applied to rotate the fetal pelvis so it can pass through the greatest diameter of the maternal pelvis in an oblique manner. Others tie the forelimbs of the dead fetus together and by placing a long handle between them will rotate or twist the fetus as a traction is applied. The use of the long blunt hook placed over the fetal ischial arch or into the caudal border of the sacro-sciatic ligament aids in placing traction on the pelvis, lifts the fetal pelvis in the maternal pelvis, and pulls the fetal pelvis in an oblique manner aiding in the relief of the dystocia. If the fetus is dead an extensive transverse incision in the abdomen of the fetus caudal to the xiphoid region followed by evisceration, insures traction being applied not to the linea alba or fetal pubis but only on the spinal column. This produces extension of the fetal pelvis on the spinal column and facilitates withdrawal of the fetus. If judicial traction fails to relieve the dystocia, fetotomy should be performed by bisection of the fetal pelvis with a fetotome. This is made less difficult by evisceration after transversely incising the abdomen.

Forward Extension of the Hind Limbs beneath the Fetal Body or the "Dog Sitting" Posture is observed uncommonly in the mare and cow. The reason for the dystocia may not at first be obvious. The cranial extremities are usually presented normally and pass into the birth canal before dystocia results. Passing the hand forward along the fetus, the operator can feel the hind feet and limbs entering the pelvic cavity alongside the fetal abdomen. This examination will serve to differentiate the condition from twins, fetal ascites, or a fetal monster such as a *Perosomus elumbis*. This condition is seen most commonly in the mare because it is possibly a vertical form of the transverse ventral presentation in which the anterior portion of the fetus became dislodged and entered the pelvis. The prognosis in the mare should be guarded to poor. Traction by laymen or veterinarians not recognizing this condition may cause severe damage especially if the hind feet are caught beneath the brim of the pelvis instead of extending into the pelvic cavity. This operation may be handled by mutation only in large mares with a small fetus, or in the cow by repelling the hind limbs into the uterine cavity as the fetus is pulled

from the vulva. Forced extraction should never be used. Fetotomy is often the method of choice and consists of detruncating the fetus with the fetatome through the posterior thoracic or anterior lumbar region. Sometimes evisceration is helpful if performed before detruncation. Often it is necessary to make two cuts through the trunk in order to remove enough of it so that the rear quarters can be manipulated. Krey's tongs placed into the exposed vertebrae assist greatly in drawing the lumbar portion of the trunk toward the vulva, in placing the fetatome wire and in removing more of the trunk of the fetus. After detruncating, chains are placed on the hind pasterns, the rear quarters are repelled into the uterus as the hind feet are drawn into the birth canal and the hind quarters are rotated from a dorso-pubic to a dorso-sacral position and then removed by traction. If necessary the pelvis may be bisected with a fetatome. In some instances cesarean section may be preferred for the correction of this serious type of dystocia.

Dystocia in Posterior Presentation is relatively much more common than dystocia in anterior presentation. Posterior presentation is considered pathological in all except the multiparous animals. The frequency of physiological birth in posterior presentation in the mare and cow is quite low. The fetal mortality in posterior presentation is high. Most authorities advise rather prompt removal of the live fetus in posterior presentation to prevent asphyxiation following pressure on or rupture of the umbilical cord. Most fetuses are usually dead at the time of the examination.

Dystocia due to Dorso-ilial or Dorso-pubic Positions in Posterior Presentation is similar in nature to, and handled by rotation in the same manner as pathological positions in anterior presentation. They are usually less difficult to correct, because the head and neck are not present to offer obstruction to rotation as in anterior presentation; and, because the rump is more rounded than the withers, rotation is easier. Occasionally, in the mare in posterior presentation, the hind feet may engage the roof of the vagina and cause lacerations of the vagina, vulva, and rectum. Lifting the fetal buttocks upward and to one side or the other aids rotation of the fetus by opposite traction on the two rear limbs. Prior to correcting the abnormal position, the operator should determine if the birth canal requires lubrication and whether torsion is present.

Deviations of the Hind Limbs in Posterior Presentation are common in uniparous animals. They are uncommon as a cause for dystocia in multiparous animals because of the latter's small, flexible limbs. These are caused by failure of the hind limbs to extend into the pelvic cavity or by the foot or fetlock catching on the

birth canal or pelvic brim, causing the hind limb or limbs to become flexed. When one joint becomes flexed all joints in the hind limb flex except when the hind leg is extended beneath the body.

The flexion of the limbs at the tarsus or "hock-flexed posture" causes the flexing of the rest of the articulations, followed by dystocia. It may be diagnosed by palpation of the perineal region and tail and then below these the point of the flexed hock either in or just below and cranial to the pelvic cavity. This condition should be differentiated from ankylosed rear limbs seen in **Perosomus elumbis**. Correction of this dystocia is easily accomplished by mutation when dystocia has not existed too long. After epidural anesthesia is administered the fetal buttocks are repelled cranially and to one side. The flexed hock is grasped and repelled forward and laterally into the opposite flank while the foot is drawn caudally and medially and extended through the birth canal (see Figure 88). The hoof or claw should be guarded or cupped in the hand as it is brought back over the pelvic brim so that it does not catch and lacerate the soft structures of the uterus or birth canal. If the dam is recumbent the rear parts should be elevated above the fore parts and the flexed fetal limb should be in the upper flank of the dam so that room is available for mutation and so that the weight of the fetus does not rest upon the flexed limb. In cases of a very large or an emphysematous fetus, or a contracted uterus that will not allow repulsion and room for mutation, or in recumbent cases in which mutation is very difficult, fetotomy with amputation of the rear limb at the tarsus may be necessary and is simple to perform with the fetatome. Rarely in the mare the flexed rear limb may become wedged in the pelvis with the hock impacted against the sacrum and the fetlock against the floor of the pelvis. Amputation of the tarsus is the safest procedure to follow as it prevents further laceration or contusion of the birth canal. Occasionally the rear limbs will have the stifles flexed with the tibias impacted against the pelvic brim. Repulsion of the fetus, lifting the femorotibial joint upward with the hand, as traction is exerted on the pastern, will remove this cause for dystocia.

Complete Retention or Extension of the Rear Limbs beneath the Body, or Breech Presentation is observed frequently as a cause for dystocia in animals. This is a more advanced case of retention of the rear limbs than the hock-flexed posture. The rear limbs are usually completely extended beneath the fetus. The buttocks and tail are in the pelvic cavity and occasionally the tip of the tail is hanging from the vulva. In many cases no part of the limb can be reached until the fetal buttocks are repelled cranially out of the pelvic inlet. Epidural or gen-

eral anesthesia is very helpful or necessary. By grasping the cranial aspect of the tibia with the hand or passing a chain around the tibia the operator can pull the fetal leg back into a hock-flexed posture as the fetal hind quarters are repelled forward and upward. If this is possible the procedure is the same as outlined previously (see Figure 88). If, however, the fetus is dead, emphysematous, or large, and the uterine wall has contracted around the fetus so that room for mutation is not available, fetotomy is indicated. Forced extraction is seldom indicated, warranted, or necessary. Bisecting the fetal pelvis in breech presentation in posterior presentation is easily performed with the fetatome by passing the fetatome wire around one hind leg, placing the head of the fetatome on the opposite hip and making a diagonal cut through the fetal pelvis. In multipara forceps may be applied across the fetal hips after lubrication and the fetus removed by traction; or the hind limbs may be extended into the birth canal and traction applied by a snare, or manually with gauze wrapped around the rear legs of the fetus. Excessive traction in multipara is to be avoided. In severe or prolonged dystocia in multipara, cesarean section or hysterectomy may be indicated.

Hip Lock in Normal Posterior Presentation is occasionally a cause for dystocia, especially in heifers. In posterior presentations, uterine inertia or delay in the second stage of labor are commonly observed. For this reason, in many cases traction is applied successfully by laymen, or the veterinarian may be called to effect a simple delivery with the fetus in posterior presentation, and its hind limbs lying in the birth canal. This should not be termed, or confused with, true hip lock, where, as in anterior presentation, the width of the fetal pelvis at the level of the greater trochanters is greater than the bisiliac diameter of the maternal pelvis. In hip lock in the posterior presentation, the fetus should be repelled and lubricated, if necessary. Traction should be applied to only one rear limb at a time. Some veterinarians will tie the two rear limbs together, place a long handle or their arms between them and rotate and twist the hips as traction is applied. This causes the fetal pelvis to pass through the maternal pelvis at an oblique angle or in a dorso-iliac position necessary to effect a correction of the condition. If this fails, because of the large size of the fetus or the small size of the maternal pelvis, or both, then cesarean section or fetotomy should be considered. If the fetal hips can pass through the pelvis, little difficulty will be encountered with the chest and pectoral girdle. In rare cases fetal ascites may cause dystocia in posterior presentation, simulating a hip lock condition. In dystocia due to severe hip lock, if the fetus is alive and the birth canal small, cesarean section should be given serious

consideration. If the birth canal is relatively large and the fetal size not excessive, fetotomy may be the procedure of choice. This is accomplished by amputation of the rear limb at the hip joint or preferably by bisecting the pelvis with the fetatome, as previously described under fetotomy.

Dystocia due to Bicornual Pregnancy or Transverse Presentation is rare and is seen most commonly in the mare. In rare instances it may occur in all species except swine, in which it has never been reported. The incidence of this type of pregnancy was reported as 1 in 1000 equine births.³⁵ This author believes it may be even more rare. Some bicornual pregnancies might possibly undergo spontaneous version at the time of parturition into an anterior or posterior presentation,^{41,42} but this is questioned. For a transverse presentation to occur it is essential that either a bicornual pregnancy be present or that a fetus in a normal longitudinal pregnancy become deflected at parturition across the pelvic inlet into the opposite horn. The former condition, a primary bicornual pregnancy, has been described most commonly in mares, bitches, and cows (see Figures 86 and 89). It is possible for it to occur also in ewes and queens. Secondary bicornual pregnancy may occur occasionally in multiple or bicornual pregnancy in ewes, does and cows or in bitches and queens. When a fetus is wedged in the birth canal, the next fetus may be forced across the uterine body into the opposite horn; when both horns are large one fetus may fail to enter the birth canal in a proper manner and be forced into the opposite horn. In bitches bicornual or transverse pregnancy is seen most commonly in conceptions with a single fetus that develops across the body of the uterus with the fore quarters in one horn and the rear quarters in the other horn and the dorsum toward the pelvic canal. It is suggested that this is a natural attempt of physiological forces to equalize the load of pregnancy between the two horns. Usually this single canine fetus is large. Transverse pregnancy has not been reported in swine because of the very acute angle at which the horns meet the body and the short compact body of the porcine fetus, making transverse pregnancy a near impossibility. In the cow the transversely developing fetus must assume a U-shape, with portions of the fetus in both horns. It is necessary that the dorsum of the fetus becomes convex and lies against the cervix. In cattle this condition is extremely rare. In sheep it has been observed occasionally in cases where triplets or quadruplets cause a great distention of the uterine horns, and a transverse presentation of one fetus may develop at the time of parturition. In rare cases an equine body pregnancy may occur with the fetus in transverse presentation, with only a small portion of the

cranial and caudal parts of the fetus in each horn.

Transverse Ventral Presentation is the transverse presentation most commonly observed in the mare. The limbs are extended into the uterine body. The occurrence of wry neck is common in equine fetuses developing transversely. Thus at parturition the four limbs are wedged across each other in the pelvis. The head is usually out of reach alongside the fetal body. Expulsive efforts by the mare or traction by laymen result in failure to relieve the dystocia. Due to the nature of the transverse presentation little or no damage of the birth canal or uterus usually results from these efforts. It is necessary to carefully examine the limbs to differentiate the fore and hind legs, so tightly are they impacted and wedged across each other. In certain cases the feet may protrude from the vulva. The prognosis in transverse ventral dystocia in the mare is fair to good depending upon the condition of the mare and her genital tract. Occasionally the transverse ventral presentation is somewhat oblique in presentation, with no portion of the fetus extending into the pelvis. Possibly these are partially rotated bicornual pregnancies. In these cases it is difficult or almost impossible to relieve the dystocia and save the mare without resorting to cesarean section. To correct the usual transverse ventral pregnancy, mutation alone—by repelling the fore parts and applying traction on the rear limbs as the forelegs are flexed and repelled along with the fore parts—can be accomplished only when the fetus is small and the uterus and birth canal are relaxed and large. Epidural analgesia or general anesthesia is usually necessary. The generally accepted manner of relieving this type of dystocia is to remove the forelimbs by amputation at the humero-radial joint with the fetatome. It may be necessary or advisable to amputate the rear limbs at the tarsus in order to provide room for amputating the forelimbs. By applying traction with rotation of the rear limbs and repulsion on the fore quarters or sternum, the fetus is turned by version and rotated into a posterior dorso-sacral position. With the fetus in a posterior presentation the fetal head and usually wry neck do not cause difficulty for the operator. Aftercare of these bicornual pregnancies in the mare is important, as metritis and vaginitis are likely to develop.

The Compound or Rotated Bicornual Pregnancy is of rare occurrence in the mare. It is basically a bicornual pregnancy, usually ventral, that during the latter stages of gestation rotates so that the fetus comes to rest beneath the elongated vagina and uterine body. The dorsum of the uterine horns is ventral and the ventral portions of the horns lie dorsal to the fetus, with the legs of the fetus pointing cranially and dorsally. This rotation of the two horns may be nearly a complete 180 degrees.

At the time of parturition the birth canal is very long and the elbow may be the only portion of the fetus that can be reached by the operator. The rest of the fetus may be palpated through the long narrow birth canal, below the hand and arm. For this reason it may occasionally be confused with an extrauterine fetus. Occasionally the rotation may not be through 180 degrees, and the fetus may be resting on its back, as the uterine horns have rotated only 90 degrees; but here too the birth canal is long and narrow, offering a serious obstacle to birth. In the author's limited experience on only 6 to 10 of these rotated bicornual pregnancies, the mare in most instances had a history of dystocia or retained placenta the previous year. Another report did not confirm this association.³⁵ The symptoms of dystocia in these rotated bicornual transverse presentations are mild, resembling the first stage of labor. Tenesmus or straining is absent or slight because the fetus does not enter the pelvic canal and stimulate labor. In this respect it resembles torsion of the uterus. By the time the veterinarian is summoned to examine the mare, in many instances 24 to 48 hours after the onset of parturition, the uterus is well-contracted and the fetus is often emphysematous. A cesarean operation offers the only hope for saving the mare with this type of dystocia. The prognosis is usually guarded. In many cases consultation may be desirable whether the mare is destroyed or a cesarean operation performed. Fetotomy is impossible because of the stretched narrow, long birth canal.

Transverse Dorsal Presentation is very rarely observed in the mare but usually occurs in the rare transverse pregnancies in ruminants and carnivora because of the sharp angle at which the two horns leave the body. In cases which have had an early diagnosis, mutation may be performed by repelling one end of the fetus—preferably the cephalic portion—and by putting traction on the opposite, or caudal extremities of the fetus by means of chains, Krey's hooks, or a blunt hook inserted through an incision in the skin. If version of the fetus into a posterior presentation cannot be brought about then version into an anterior presentation should be attempted. When mutation fails fetotomy is often successful in the large animals and is accomplished by passing a fetatome wire around the fetus in the lumbar region and bisecting the fetus so each half may be removed separately. If this cannot be done with the fetatome then the skin over the lumbar region should be incised transversely, the back bone broken with a chisel, and the fetus eviscerated. The fetatome wire may then be passed around the collapsed body of the fetus and the body divided and removed. In the bitch mutation is usually impossible and cesarean section is the method of choice.

This may also be decided upon the the cow and mare.

Dystocia Due to the Umbilical Cord and Placenta—Dystocia caused by the cord being wrapped around a portion or extremity of the fetus does not occur in domestic animals. Occasionally the umbilical cord may be found around a leg, especially a rear leg, of the fetus. In this position it will usually rupture before causing dystocia. Thus it may be the cause for the death of the fetus by asphyxia. The belief that amputation of the fetal limbs can be caused by the umbilical cord being looped around them is erroneous. A bovine dystocia due to a very thick amnion that required incising to deliver a normal live calf has been described.²¹ This appeared to be a vascular lesion involving the entire amnion as little edema was present.

Dystocia Due to Abnormal Size of the Fetus

Dystocia may occur as a result of fetal giantism, excessive volume of parts of the fetus, excessive volume of the fetal fluids (hydrops), fetal monsters, and multiple births in uniparous animals.

Fetal Giantism is observed only in rare instances in domestic animals. True fetal giantism is seen most commonly in the cow and occurs only as a result of a prolonged gestation period of over 300 to 310 days. True fetal giantism with prolonged gestation has been reported only very rarely in other domestic animals. In mares that carry foals 365 days the foals are not excessively large. An inbred herd of Holsteins and an Ayrshire herd have been described,^{18,23,43} in which fetal giantism was due to a simple recessive hereditary factor. This condition has been described in other breeds of cattle.^{16,17} The cows carried their fetuses over 310 days. The fetuses were excessively large and the cows showed no signs of pelvic relaxation and little or no mammary development prior to parturition or at the time that normal parturition was expected. All the calves died shortly after birth even when a cesarean operation had been performed. These calves had possible anterior pituitary gland abnormalities, hypoplastic adrenals and an abnormal glucose metabolism.²² Most fetal giants have long hair, long hoofs, and the incisor teeth are well-erupted. In many cases hairballs may be found in the amniotic cavity. Fetal giants are poorly viable and often male. When a bovine fetus weighs over 130 lbs. it may be termed a fetal giant. Prolonged gestation does not necessarily indicate the presence of fetal giantism. In cases of excessively prolonged gestation in Guernsey cattle¹⁹ (See Duration of Gestation and Initiation of Parturition) most fetuses are small,

immature and pathological and in some cases mild hydrops of the amnion and allantois may occur. Dystocia in these cases is uncommon and not severe.

Prolonged gestation may also rarely occur in cattle and other species associated with congenital defects of the head such as hydrocephalus,¹⁷ with cerebral hernia, or a Catlin mark, with a reduced size of the cranial cavity and in ewes grazing on *Veratrum californicum* resulting in fetal cyclopia and often associated giantism. These animals have an abnormal or hypoplastic pituitary gland and hypoplastic adrenals. As mentioned previously normal or increased amounts of glucocorticoids are necessary in these species to initiate parturition. When this does not occur gestation is prolonged and the fetus continues to grow in size. Oversized lambs weighing more than 20 pounds are occasionally described.¹⁵ Prolonged gestation and oversized lambs were reported in Karakul sheep in Southwest Africa.⁸ In these cases of prolonged gestation and fetal giantism in sheep and those in cattle the fetus in many cases dies after a variable period and then a number of days later the dam attempts to expel it. In many cases the pelvic cavity and genital tract is not properly relaxed, there is a lack of fetal fluids, udder development is often lacking and severe dystocia occurs. In a few cases beginning mummification of the large fetus may begin before the fetus is expelled. In cows and ewes the mortality is high due the severe dystocia, uterine inertia, septic metritis, and retained placenta.

The condition of fetal giantism should be carefully differentiated from a large fetus, especially in the large breeds of cattle, causing dystocia due to fetopelvic disproportion at the end of a normal gestation period when the relatively small size of the birth canal makes the large fetus seem a "giant." This latter condition, resulting in dystocia, may occasionally be handled in a mature cow by forced extraction. Percutaneous total fetotomy might be considered in selected cases.^{6,44} If the birth canal is small and underdeveloped or not relaxed, and the fetus emphysematous, fetotomy is extremely difficult or impossible to perform. Cesarean section should be considered. Under certain conditions slaughter might be recommended.

If fetal giantism is discovered or suspected at 280 to 300 days of gestation, and parturition does not seem imminent, a daily dose of 15 to 20 mg. estradiol alone or together with 20 to 40 mg. of dexamethasone or 5 to 10 mg. of flumethasone repeated daily or every third day and possibly combined with 25 to 40 mg of prostaglandin F_{2a} might be indicated to induce parturition or abortion. Large repeated doses of estrogen, such as 60 to 240 mg. of stilbestrol every 24 hours, resulted in 13 to 16 cows calving within 2 to 5 days.³⁷ These were cases of

prolonged gestation, where the fetuses had been carried 9-1/2 to 12 months. Lactation was not affected in most of these cattle so treated. (See Artificial Induction of Abortion.) When parturition is artificially produced the cow should be observed carefully so that aid may be given if necessary. Cesarean section might be used to terminate the prolonged pregnancy; however, metritis and retained placenta invariably complicate the treatment. Slaughter should be seriously considered in dairy cattle since milk production is greatly reduced.

Dystocia Caused by Excessive Size of Parts of the Fetus may be due to rare instances of hypertrophy of any gland; a tumor such as a melanoma, sarcoma or others (see Tumors of the Newborn); a pathological enlargement or cystic dilation of any hollow or secreting organ or structure due to an anomaly in development causing a stenosis or an obstruction to the release of fluid. Reports show that dystocia may be due to an enlarged fetal thyroid, thymus or kidney, polycystic kidney, cystic dilation of the ureter,³⁰ hydrocephalus, distention of the rumen in a *Schistosomus reflexus* monster or fetal ascites. If forced extraction is not successful, incision of the abnormal glands or cystic enlargements to allow the escape of the soft parenchyma or fluid will usually relieve dystocia due to these causes. Except in cases of hydrocephalus and ascites further fetotomy is seldom required. In a few unusual cases cesarean section might be indicated.

Dystocia caused by a Disparity between the Size of the Normal Fetus and the Maternal Pelvis, Fetopelvic Disproportion. These dystocias occur usually in primipara in which the fetus may be slightly larger than normal or the pelvis may be slightly smaller than normal, or both causes may be present. Male calves are carried slightly longer and weigh 5 to 10 pounds more than female calves. Thus male fetuses are frequently present in these dystocias. As discussed under the basic causes for dystocia, crossbreeding of certain breeds and breeding heifers to certain bulls may predispose to dystocia. If primiparous animals are not grown well by proper feeding and management practices or are bred too young, the size of the pelvis at parturition may not be adequate.

In these mild to moderate disparities between fetal size and maternal pelvic diameters, application of moderate forced extraction is indicated when the fetus is in a normal presentation, position and posture for birth and the genital tract, especially the cervix, has dilated to its fullest extent. Delaying assistance by traction for too long may result in a dead fetus or an exhausted dam. In some cases added lubrication may be desirable. Traction should be in the proper direction. Alternate traction as well as lateral traction should be used. Twisting or rotation of

the fetus may be helpful. If excessive traction is to be used epidural anesthesia should be given. If traction is not successful, early consideration of cesarean section should be given in order to save a living fetus. Fetotomy is less commonly indicated in animals with a narrow birth canal and a large fetus. But percutaneous total fetotomy might be considered if the birth canal is not too small.^{6,44}

Dystocia may be caused by Dropsical Conditions, such as Fetal Ascites, Fetal Anasarca, Edema of the Allantois Chorion, and Hydrops of the Amnion or Allantois or both. Fetal ascites is seen as an occasional cause for dystocia in any species but occurs most often in the cow. It is occasionally associated with a dropsical condition of the uterus, mesotheliomas of the fetal abdomen, and has been observed associated with brucellosis. The fetus is usually fairly small but the distended abdomen causes it to become wedged in the pelvic inlet. (See Figure 91.) It might be confused, therefore, with the hip lock condition. Close examination of the fetus in the birth canal will readily reveal the cause for the dys-

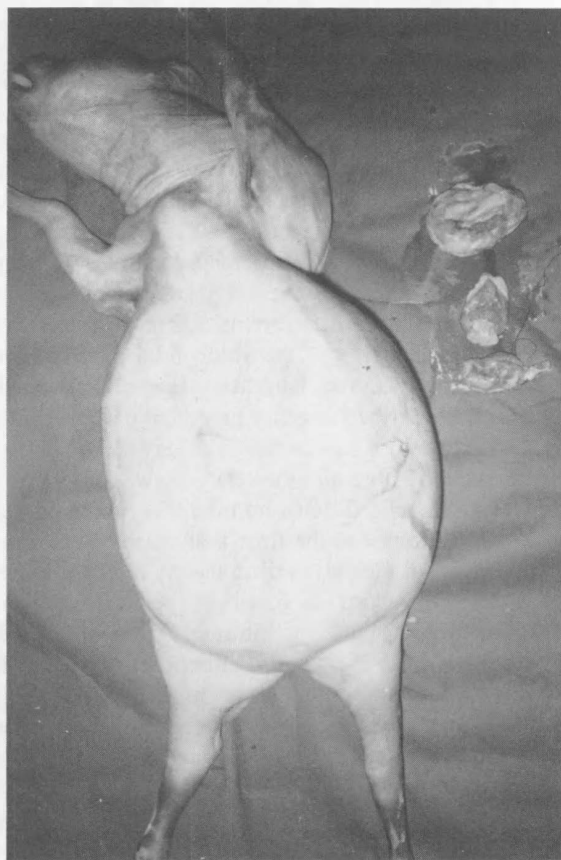


Figure 91. Ascites and mild anasarca of a 6-month bovine fetus that caused dystocia.

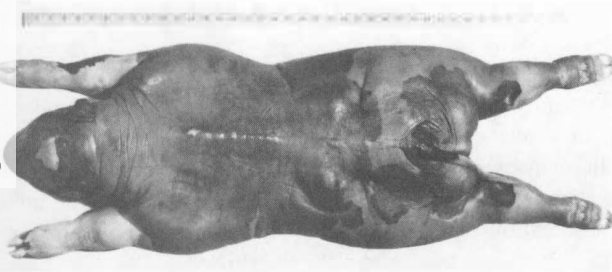


Figure 92. An anasarous bovine fetus that caused dystocia at the time of abortion.

tocia. To release the fluid from the abdomen the fetus must be sacrificed but this is no great loss as these fetuses are usually dead or weak or would fail to survive if delivered alive. The easiest method is to reach in alongside the fetus and with a castrating knife make a liberal incision through the abdominal wall. In anterior presentation a foreleg could be removed and evisceration would release the ascitic fluid.

The other dropsical conditions of fetal anasarca (see Figure 92), edema of the allantois chorion, hydrops amnii and allantois, and hydrops allantois were discussed in Chapter 5. In removing large anasarous fetuses, forced extraction is usually successful. If the fetus is too large, fetotomy including amputation of the forelimb and evisceration may occasionally be necessary. This is easily performed because of the soft, friable, edematous fetal tissues. Rarely cesarean section might be indicated. In these dropsical uterine conditions uterine inertia and a weak or dead fetus frequently occur and favor abnormal postures, emphysema and dystocia that can usually be relieved by mutation and forced extraction.

Twining in Uniparous Animals is a Common Cause of Dystocia. This is produced by portions of bicornual fetuses becoming wedged in the maternal pelvis. Dystocia is predisposed in unicornual twins because of the inertia of the long, distended uterine horn bent at a 180-degree angle at the diaphragm. Uteri containing multiple fetuses in unipara are prone to develop uterine inertia and uterine disease. The fetuses are less viable. These latter factors usually produce abnormal postures. In many cases one fetus presents anteriorly and the other posteriorly, the latter often in breech presentation. Dystocia due to twins is most common in dairy cows, and less common in beef cattle. Twin dystocia is uncommon in the mare inasmuch as twins almost always are aborted. Sheep have adapted themselves to two fetuses and twin dystocia is uncommon by comparison with the incidence of twins in that species. Twin dystocia usually may be diagnosed readily on examination of the birth canal by

finding three or more limbs attached to two separate fetuses. Diagnosis should differentiate between this condition and double monsters, *Schistosomus reflexus*, campylorrhachis, or dystocia in anterior presentation with the hind limbs extended alongside the body. If twins are wedged in the birth canal usually traction is placed on the twin nearer the vulva. The other fetus is repelled at the same time. Since twin fetuses are small, mutation is invariably successful. Conditions of twin pregnancy and dystocia may be followed by metritis and retained placenta. In cases of unicornual twin dystocia it occasionally happens that one twin is removed and the other overlooked. The same may happen in triplet pregnancies. Thus following all dystocias the uterus should always be examined carefully to be certain no fetus is left in the uterus.

Dystocia due to Fetal Monsters. The relative incidence of fetal monstrosities by species is reported as follows:

Table 15. Relative incidence of fetal monstrosities.

	Craig (citing Gurlt)	Williams	Roberts
Cow	239	15	92
Ewe	179	1	2
Sow	87	1	2
Bitch	78		
Cat	71		
Mare	56		3
Goat	24		2
Total	734	17	101

According to other authors, out of 2340 foals in one stud, only 9 were monstrosities; in cattle about 0.5 per cent; and in sheep 1 in 768 lambs were anomalous.⁷

Not all anomalous fetuses or monsters cause dystocia. The monsters that are characterized by an increased size of the fetus include: hydrocephalic, anasarous, or ascitic monsters; monsters with marked skeletal defects such as *Schistosomus reflexus*, *Campylorrhachis scoliosa*, *Perosomus elumbis*; monsters due to conjoined twins or double monsters; monsters due to pseudo-ankylosis of the limbs or neck; achondroplastic fetuses with short, broad bodies; and mummified fetuses that died late in gestation. Other anomalous fetuses that are weak or dead at birth may cause dystocia due to abnormal positions and postures because of their lack of movement and muscle tonus. If these latter defective, malformed, non-viable fetuses cause dystocia they can usually be removed by mutation and forced extraction unless emphy-

sema or marked contraction of the uterine wall has resulted.

Among the author's cases the incidence of dystocia in cattle due to excessive size of the fetus was as follows, in order of frequency: **Schistosomus reflexus**, 14 cases; **Perosomus horridus** (Gurlt) with ankyloses of the limbs and a short S-curved spine 13 cases; **Perosomus elumbis**, 5 cases, double monsters, 3 cases (two Thoraco-abdomino-pagus, one Dicephalus); fetal anasarca, 2 cases; **Achondroplasia**, 2 cases; and **Hydrocephalus**, 2 cases. Hydrocephalus is occasionally seen also in equine, porcine, canine and feline fetuses. Most single fetal monsters weigh less than normal fetuses, so they are easily handled.

In a dystocia case a careful examination of the fetus should be made for signs of a monster such as: deformed limbs, ankylosed thin limbs with prominent joints, improper placement or location of extremities, atrophied muscles and small fetal size. This examination is particularly important in differentiating between twins and double monsters. When traction or repulsion is placed on one portion of the fetus and the opposite part also moves, either a double monster or a sharply-bent single monster is present. In other cases of dystocia when proper and normal progress toward the correction of the dystocia ceases the fetus should be carefully reexamined for the possible presence of a monster or an anomalous condition.

In the handling of dystocia due to monsters each case is an individual problem. The operator must rely on a careful examination of the fetus and birth canal and on his own ingenuity and ability to plan a procedure that assures a satisfactory outcome. If the condition is severe and complicated extra assistance and even consultation should be obtained. Double monsters occur most commonly in the cow, sow, bitch, and queen, and only very rarely in the mare. Fetotomy, including evisceration, is usually indicated to reduce the size of the monster to the point where the fetatome wire may be placed around conjoined twins at the point of attachment and separate them for removal. A cesarean section to relieve dystocia due to excessive size of the fetus requires a large abdominal incision that may complicate the operation and aftercare.

Hydrocephalus is seen most often in the cow, bitch, queen and mare and when it is severe enough to result in a dystocia that cannot be relieved by mutation and forced extraction the soft portion of the distended cranium should be reduced in size by an incision to release the fluid. An excessive bony enlargement of the cranium may require that a cephalotomy be performed with the fetatome, by placing the wire around the base of the en-

larged skull, amputating and withdrawing the collapsed cranial bones and tissues.

An achondroplastic calf generally can be removed by traction with a chain looped around its neck. Lubrication is of vital importance in severe cases. The limbs are quite short and small and cause little trouble. In cases associated with fetal emphysema, removal of the foreleg and evisceration of the fetus may be indicated. This applies also to anasarca calves (see Figure 92). The latter are usually aborted prematurely and their tissues are soft and easily mutilated for the purpose of releasing fluid in order to reduce the size of the fetus. Fetal ascites often is associated with this condition.

Schistosomus reflexus (see Figure 43) is seen in cattle and occasionally the sheep, goat, and pig but never in the other species. It may be presented in the birth canal in a ventral manner, with the viscera easily palpable. When examining these monsters in this presentation, the operator may be startled to feel viscera and even a beating heart. The fetal viscera might be mistaken for the dam's viscera, and a diagnosis of a ruptured uterus may follow. This mistake will be avoided by a careful examination of the fetus. The dorsal presentation of the *Schistosomus* monster consists of the head and the four feet extending into the pelvic cavity. Since many of these monsters are small they may be removed by careful traction especially from adult dairy cows with a large pelvis. In the ventral presentation hooks or Krey's tongs may be used for traction. In dorsal presentation alternate traction on the legs is sometimes successful in relieving dystocia. In many cases, however, fetotomy is indicated. It is desirable to cut the body in half at the point of the greatest ventral curvature of the spine. Every effort should be made to place the fetatome wire around the middle of the fetus and between the front and hind limbs before the actual cutting operation. In some large fetuses after removing the head, forelimbs, and part of the thorax, it may be necessary to bisect the pelvis before the dystocia can be relieved. In rare cases a sac of skin may completely enclose the limbs and must be incised and the enclosed fluid released before starting the fetotomy (see Figure 43). Cases of dystocia in this type of monster associated with a greatly distended rumen have been observed by the author and others.^{14,41,42}

Campylorachis scoliosa is rarely observed but is handled similarly by cutting the body into two halves with the fetatome. **Perosomus elumbis** if in posterior presentation may be mistaken for a breech presentation. This abnormality is seen most often in cattle and pigs. In anterior presentation the rigid ankylosed hind limbs may obstruct the passage of the caudal portion of the fetus through the maternal pelvis. Since the fetus, es-

pecially the rear quarters, are small, atrophied, and loosely attached to the trunk, correction of the dystocia by mutation and careful traction can be accomplished in many instances. Occasionally amputation of the rear limbs at the tarsus or hip with the fetatome may be necessary in order to remove the fetus without endangering the dam.

Perosomus horridus with general ankylosis or muscle contractures of the fetus is an occasionally observed anomaly in cattle in New York State. The monster, usually a Holstein, is small and very short due to an S-shaped multiple bending of the spine from the occiput to the sacrum. The vertebrae are definitely abnormal, shortened, and ankylosed. The limbs, neck, and tail are ankylosed and deformed. Due to the small size of the fetus, however, the dystocia is usually relieved by traction.

In any of the above types of dystocia due to monsters with the exception of the achondroplastic or anasarctic calves, pseudo-ankylosis of one or more joints or limbs is common. If fetotomy does not give promise of success, cesarean section would be indicated; but the abdominal incision will necessarily be large unless fetotomy can be performed on the fetus *in utero* before its removal through the abdominal incision. Most of these animals will conceive on subsequent breeding and produce normal young unless complications following the dystocia cause pathological conditions that delay or prevent conception. In the sow, bitch, and queen cesarean section is the method of choice and often is necessary in order to relieve dystocia due to a fetal monster.

Dystocia Due to Uterine Displacements

Dystocia may be caused by uterine displacements such as uterine torsion, displacement of the uterus in inguinal or ventral hernias, rupture of the prepubic tendon, folding of the uterus cranial to the pelvis in older deep bodied sows and possibly vagino-cervical prolapse.

Uterine torsion as a cause of dystocia is uncommon in the mare, however one report indicated that 5 to 10 percent of all serious dystocias in mares were due to torsion of the uterus.³⁶

Dystocia due to Uterine Torsion is frequently observed in cattle, especially dairy cattle confined for long periods in the stable. It is occasionally observed as a cause for dystocia in ewes, does, mares, bitches and queens and in rare instances in the sow (See Figure 93). As noted in Chapter 5, in which the etiology, symptoms, and diagnosis of torsion of the uterus in the preparturient animal were discussed, about 90 percent of torsions of the uterus in cattle are observed at parturition and cause dystocia. Whereas in the other species, except possibly

the occasional ewe or doe, most uterine torsion occurs with symptoms during the latter third of the gestation period prior to parturition.^{3,25} Torsion of the uterus as a cause of dystocia was present in 7.3 and 7.0 percent of 1555 and 998 cases of bovine dystocia observed in the Ambulatory Clinic of the New York State Veterinary College from 1943 to 1953 and 1963 to 1968, respectively. Records from the same clinic from 1925 to 1945 showed that of 1703 cases of bovine dystocia, 225, or 13.2 percent, were due to uterine torsion.⁴² In other countries the incidence varies from 1 to 12 percent.³⁴ About 70 percent of torsions occur in cows and 30 percent in heifers. This is probably a reflection of the numbers of pregnant cows at risk. Uterine torsion is apparently rare in **Bos indicus** type cattle due to the anatomical attachment of the uterine ligament.³⁴ The condition is observed most frequently in stabled cattle during the spring months. Apparently most cases of torsion occur during the first stages of labor. Torsions to the right are usually associated with fetuses in the left horn and viceversa.^{3,34} Most twisted uteri are outside the omentum that usually encloses the uterus. The degree of torsion varied from 90° to more than 720° with 80 percent of the cases between 180° and 270°^{33,34} or more. Uterine torsion is rare in twin pregnancies.

The symptoms of uterine torsion of the cow occurring at the time of parturition and resulting in dystocia are frequently so mild that the owner thinks the cow is still in the first stage of labor. The cow is uneasy, restless, may show colic by treading, kicking at its abdomen, and switching its tail. Moderate anorexia is present. Tenesmus, or abdominal straining characteristic of the second stage of labor, is either absent or mild and intermittent because the twisted birth canal prevents the entrance of the fetus into the pelvis—a necessary prerequisite to the initiation of normal abdominal straining. The history given by the owner is usually that the cow had acted as if calving was imminent for the past 8 to 18 hours or more, but true labor or straining has not occurred. This history of a prolonged first stage of parturition is usually observed in uterine torsion causing dystocia and is significant when an owner observes his parturient cows closely.

Examination of the cow reveals increased respirations, and the heart rate is usually elevated to 80 to 100 per minute. In advanced cases with complications of uterine gangrene, uterine rupture, or fetal emphysema, the animal may be toxic, with a very rapid, weak pulse, severe depression, weakness, prostration, low body temperature, cold extremities, and possibly a fetid diarrhea. Hemorrhage from ruptured uterine vessels, occasionally occurs in uterine torsion and causes the cow to exhibit symptoms of anemia, weakness, rapid breathing, rapid

pulse rate, and prostration. In some severe 270° to 360° torsions in cattle it may be noticed that the dorsal commissure of the vulva is pulled forward and to the left or right, depending upon which direction the uterus rotated. An accurate diagnosis of uterine torsion may be made by vaginal and rectal examination of the uterus, broad ligaments, vagina, and fetus, as described in Chapter 5 (see Figure 93). Whenever the birth canal is narrow and stenosed in the region of the cephalic portion of the vagina or the cervix at the time of parturition, torsion should be suspected. If the torsion is greater than 180° to 240° it is usually impossible to pass the hand through the twisted portion of the birth canal. This twisted portion usually includes the cephalic portion of the vagina, the cervix, and occasionally the body of the uterus. Frequently in the mare, but rarely in the cow, the torsion may be entirely cranial to the cervix so a vaginal examination is not as highly diagnostic in the mare as it is in the cow.^{25,36} Epidural anesthesia is usually necessary, as oftentimes this examination initiates severe straining. The fetus is usually in a dorso-ilial or dorso-pubic position as most torsions in cattle are 180° to 240°. The fetal membranes may have ruptured. The fetus is likely to be dead, and long-standing neglected cases of dystocia may show evidence of emphysema or maceration. In all cases of dorso-ilial or dorso-pubic positions of fetuses in unipara the birth canal should be carefully examined for the presence of a torsion. The incidence of uterine rupture is fairly high in cases of uterine torsion and therefore an examination for this should be made prior to treatment. The direction of the torsion should be carefully ascertained. Torsions in the mare and cow of 180° or less during the gestation period may recover spontaneously.

The symptoms in the mare and ewe are similar to those in the cow. In the mare the foal is usually dead and often the symptoms are mistaken for colic or indigestion. Torsions of the uterus greater than 180° are fairly common in the mare. In the ewe the fetus cannot be directly palpated, due to the twisted narrow birth canal. In multipara, such as the bitch, parturition progresses with the fetuses being expelled from the normal horn and in some cases from the caudal or patent portion of the horn in which torsion may have occurred. Unless the abdomen is palpated fetuses in the twisted or rotated horn or portion of a horn that may be still attached to the rest of the uterus or rarely separated from it will not be noted. Transverse rupture of this uterine segment may release the fetuses into the abdominal cavity. In 24 to 48 hours, the bitch will show depression, anorexia, elevated temperature, and rapid pulse, with symptoms of abdominal involvement by a tense, firm abdomen, arched back, and a slow, painful gait and attitude. The extrauterine fetuses

may be diagnosed by radiographs or palpated through the abdominal wall. In rare instances, especially in the queen, the twisted segment of the uterus containing one or two fetuses, isolated or separated from the rest of the uterus due to torsion of the uterus, may be walled off in the abdominal cavity by connective tissue causing the fetuses to macerate or mummify.

The prognosis of uterine torsion causing dystocia is usually fair to good when the condition is diagnosed early, before the occurrence of fetal emphysema, secondary contraction of the cervix, uterine ischemia, necrosis, rupture and peritonitis. In the 113 cases of bovine uterine torsion occurring in the Ambulatory Clinic from 1943 to 1953 there was an 11 percent mortality of the dams. In 70 cases of uterine torsion treated from 1963 through 1968 in the same clinic there was only a 4.3 percent mortality. A series of 225 cases of uterine torsion were reported⁴² from 1925 to 1945, in which an 18 percent mortality resulted.

In 42 cases of equine uterine torsion, 5 to 10 percent were associated with serious dystocias but more than 50 percent occurred before the end of gestation.³⁶ Most equine cases of torsion were 360° or more, usually to the left. Thus the prognosis is guarded for the dam and fetus with 40 percent mortality in the dams and 70 percent in the foals. Correction was best accomplished in the standing mare by rotation of the fetus and uterus through the genital tract. If this was not possible, correction through a laparotomy rather than rolling was preferred.³⁶ In very serious cases cesarean section was the method of last resort. In an excellent recent review of 26 cases of equine uterine torsion, the mean duration of gestation at the time of diagnosis was 9.6 months with a range of 8 months to term.²⁵ Torsions were clockwise in 59 percent of cases and 23 percent had torsions of 360° or more. Uterine rupture was diagnosed in 4 cases. Correction was by left or right flank laparotomy in the standing mare. Of the foals alive at surgery 70 percent were born alive. Of the 26 mares operated on 73 percent survived, 7 died from peritonitis, shock, or hemorrhage.

The prognosis in the other smaller species is guarded to poor because an early diagnosis is difficult or impossible to make without an exploratory laparotomy operation. The prognosis in respect to the life of the fetuses is poor, since in most cases veterinary aid is not summoned until too late and the fetuses, having a reduced oxygen supply, are less viable and die due to asphyxia. In torsion of the uterus with an extensive rupture of the uterus, hemorrhage from the uterine vessels or severe uterine edema and gangrene secondary to thrombi in the large uterine vessels, the prognosis is poor, especially when the latter condition is present in large animals. In

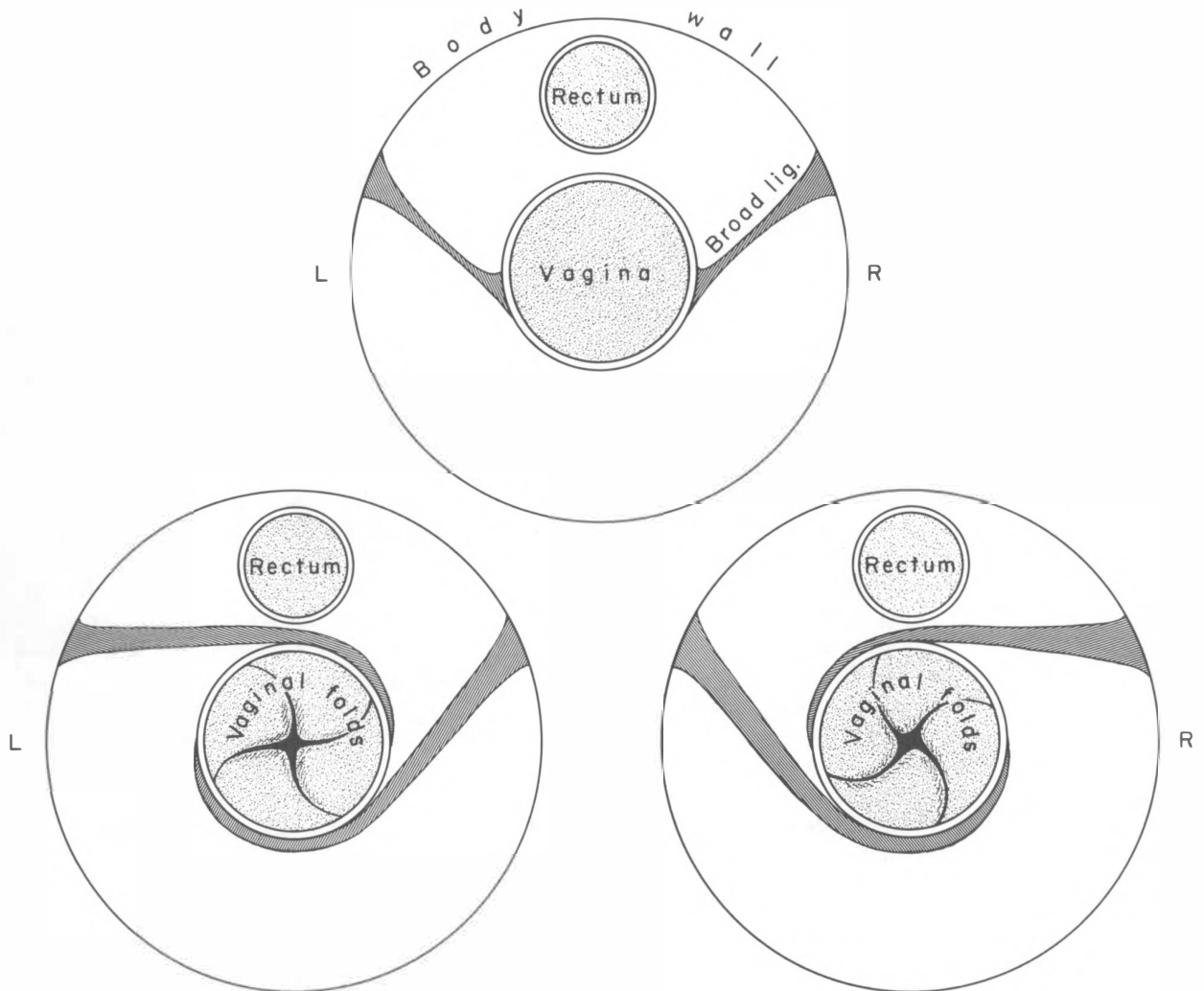


Figure 93a. Diagram of a normal and twisted bovine uterus and vagina. (Upper center) Normal position of broad ligaments and vagina. (Lower left) 180° right torsion of the uterus. (Lower right) 180° left torsion of the uterus.

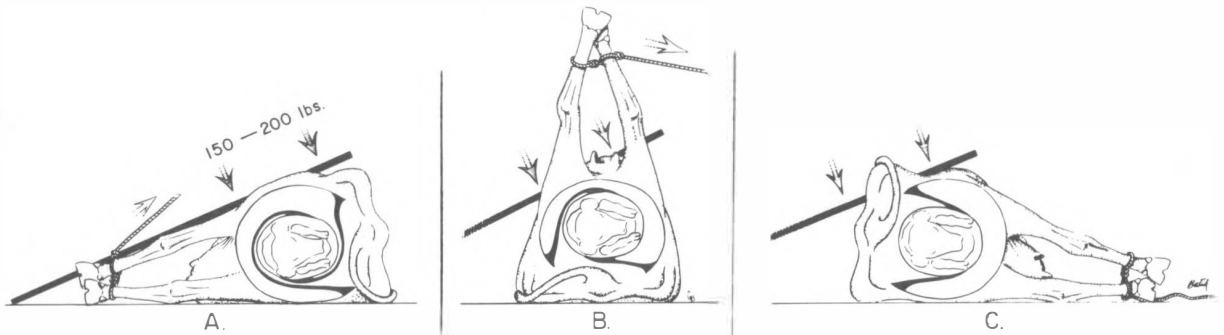


Figure 93b. The Schaffer method for the correction of right uterine torsion. A. The cow is cast on the right side corresponding to the direction of the 180° right uterine torsion, note the position of the right mesometrium. A plank and weight of 75 to 100 kg (black arrows) are applied over the abdomen. B. The cow is rolled slowly to the right in the direction of the uterine torsion. C. Rolling is completed, with the correction of the uterine torsion.³¹ Courtesy of the Cornell Veterinarian.

the bitch and queen hysterectomy may be successful if shock and peritonitis can be controlled. Most cases of unrelieved uterine torsion of greater than 180° result in the death of the dam. In rare cases the fetus remains in the uterus and macerates, with extensive adhesions developing around the uterus; and the condition may not be diagnosed for several months. Uterine torsion in cattle is likely to be followed by retained placenta, metritis, perimetritis, and delayed conception. Only rarely does torsion recur at the following parturition.

The handling or treatment of dystocia caused by uterine torsion in large animals includes several techniques, such as cesarean section, rolling the dam, and rotation of the fetus and uterus through the birth canal or through a laparotomy incision. These treatments and the modifications thereof are designed to correct the torsion of the uterus and to remove the fetus. The techniques of laparotomy, cesarean, and rolling are indicated when the birth canal is so twisted usually more than 240° and the hand cannot be passed through it to grasp the fetus, or when the cervix is not dilated, as may occur in torsion during the gestation period.

Rolling the dam is one of the oldest and simplest of the various methods used to relieve torsion of the uterus. Its principal drawback is that it requires the assistance of 2 to 4 men depending on the size of the cow or mare. If possible, rolling should be done out-of-doors, on a grassy, gentle slope with the cow's head lower than the rear quarters. In the winter months the barn floor, litter alley, or large box stall that are well-bedded or covered deeply with straw or hay may be used. The cow, especially if large and vigorous, should be given a large dose of tranquilizer intravenously or intramuscularly, or 0.5 to 1.0 ounce of chloral hydrate intravenously or 1.5 to 3.0 ounces orally, as a sedative 20 minutes prior to rolling. After the direction of the torsion has been determined accurately, the cow is laid down in lateral recumbency on the same side as the direction of the torsion. The squeeze method, with half hitches around the thorax and abdomen; or the Alabama technique, with ropes crossed over the back and between the hind legs, is used to force the cow to lie down. The hind leg on the side on which the cow is to be cast is pulled cranially and underneath it by a rope attached to the pastern and passed to the other side at the same time the body ropes are tightened. Occasionally this procedure of dropping the cow suddenly on the same side as the direction of the torsion relieves, or partially relieves, the condition. The hind legs of the cow are fastened together and the front legs are tied together, leaving an 8- to 10-foot end on each rope. The cow's head is held extended by a halter and rope and if necessary a nose lead. The front and hind

feet should not be tied together, because this compresses the abdominal cavity and tends to make the gravid uterus rotate with the cow. It is better not to tie the front legs in a flexed position to the body, as the cow will throw her knees apart and brace herself, thus making it difficult to roll her. The object in rolling the cow when relieving torsion is to rotate the body of the cow in the same direction as the torsion of the uterus, rapidly enough to rotate the body around, or faster than, the inert uterus and fetus. The rapidly rotating body of the cow thereby overtakes the more slowly rotating inert gravid uterus. The cow should be rapidly rotated in the same direction as the torsion, by strong coordinated pulling on the ropes attached to the forelegs and hind legs. If because of a lack of assistance, rolling cannot be done rapidly, some other method should be selected to relieve the torsion. Since this is often the case, the rolling technique of Schaffer may be utilized. After the cow has been rapidly rolled 180 degrees her body must then be either rolled back slowly to the original position or be pushed, usually slowly, over her legs and sternum so that she is once more in lateral recumbency on the same side as the direction of the torsion, ready to be rapidly turned over again. Although some authors advise the operator to keep the hand in the vagina or even to grasp the fetus, in order to hold the gravid uterus in place, this is very awkward position to assume or maintain as the animal is being rolled, and is unnecessary unless the operator is uncertain as to the direction in which the uterus is rotated. Placing the hand in the cranial portion of the vagina as rolling is performed will reveal at once, by the tightening of the spiral folds in the vagina, if the rolling is in the wrong direction. After each two or three rapid rotations of the cow's body the birth canal should be examined to determine if the torsion is corrected. If so, the spiral folds and stenosis of the birth canal have disappeared and if the cervix is dilated the fetus may be palpated with ease. Occasionally there may be a rush of fetal fluids from the uterus as the torsion is relieved. If the torsion is not relieved, this procedure should be repeated 4 to 5 more times before failure is admitted and another technique attempted. Rolling mares with torsion of the uterus often results in correction of the torsion as in cattle.^{12b} Rolling might result in rupture of the uterus or cause a rupture of a uterine vessel especially if the uterus was edematous.^{10,36}

A modification of this rolling technique, called **Schaffer's method** has been described^{3,31} (See Figure 93b). This method requires less assistance because the cow or mare with torsion is rolled slowly instead of rapidly. The mare should be anesthetized with a short-acting narcotic. The cow is cast on the same side as the

direction of the torsion and tied in a manner similar to that described for the previous rolling technique. A plank 9 to 12 feet long and 8 to 12 inches wide is placed on the cow's abdomen with the lower end of the plank on the ground. An assistant stands on the plank and the cow is slowly rolled in the same direction as the torsion by pulling on the ropes around the front and hind feet. This creates pressure first on the upper abdominal wall, then the floor and finally the opposite side of the abdomen resulting in a correction of the torsion that can be determined by examining the genital tract. If there is any question concerning the direction of the torsion, the operator, by placing his hand in the genital canal, can readily determine whether the torsion is being relieved or not as the cow or mare is slowly rolled. As in the initial rolling technique if the torsion is not relieved the first time the animal is rolled, the procedure may be repeated several times. In most cases the torsion is corrected on the first rolling. In the Schaffer method the uterus and its contents are held in place by the plank and the weight of the man or a similar weight placed on it while the animal is rolled.

Laparotomy for the intra-abdominal correction of torsion is especially valuable during the gestation period or when the cervix is closed. It is usually performed on the standing cow or mare through the left or right paralumbar fossa. This technique has the advantage of requiring less assistance than does rolling. In most cases tranquilizers or a small dose of chloral hydrate, 0.5 to 1.0 ounce intravenously and light epidural anesthesia are given to control tenesmus at the time of the operation. The right flank in the cow is anesthetized by paravertebral, inverted L block, or local anesthesia and a 6- to 8-inch vertical laparotomy incision is made. The omentum is pulled cranially if it is over the uterus. If torsion of the uterus is to the right the hand and arm are passed downward between the uterus and abdominal wall until the bottom or ventral surface of the uterus can be felt. A portion of the fetus, usually the leg, is grasped through the uterine wall and by alternately lifting and lowering the uterus it is made to rock up and down in an arc of 10 to 12 inches and finally by strongly lifting the uterus and pushing it toward the midline and downward, correction of the torsion is accomplished. If torsion is to the left the hand and arm are passed over the top of the uterus and down between the rumen and uterus. The same procedure of rocking and then rotating to the right or laterally and downward is carried out to correct the left torsion. A left flank incision is preferred in mares. The laparotomy incision then is closed securely. In rare cases in which laparotomy alone is unsuccessful because of chronic adhesions or a very large distended uterus or ru-

men, making correction impossible, cesarean section may be indicated. If at the time of parturition the cervix is not dilated sufficiently and the operator does not wish to lose a living fetus by delay, a cesarean may be performed. This may be done by enlarging the laparotomy incision. Although the torsion may be corrected before or after the fetus is removed, it is easier to relieve torsion after cesarean section. If a cesarean section in a cow is decided upon before making the right flank incision, another laparotomy site may be chosen since correction of the torsion is usually easily accomplished, even in the recumbent cow after the fetus has been removed. Torsion in the ewe and goat may be relieved by laparotomy if elevation of the animal by hanging it by the rear legs or by rolling it is not successful. The relief of uterine torsion in two sows after a laparotomy operation has been described.⁴⁰ One sow died due to hemorrhage from a vessel in the broad ligament; the other recovered following correction of the torsion and removal of the pigs.

Rotation of the fetus and uterus through the birth canal is probably the most common way of relieving dystocia due to torsion of the uterus in the cow and may be used in the mare. Since most bovine torsions, about 90 percent, are discovered at the time of parturition when the cervix is relaxed and dilated, and since most torsions are less than 240 degrees, the hand may be passed through the twisted portion of the birth canal and the fetus grasped and rotated in the standing cow. Manual rotation of the fetus and uterus through the birth canal is very difficult to perform with the cow lying down. In the mare with a 180° torsion of the uterus the cervix may be dilated and the fetus grasped. It is advisable, and in many cases necessary, to have the cow on its feet or its rear parts elevated, and enough epidural anesthetic injected to prevent straining. If the birth canal is dry, lubrication is necessary. If the fetal membranes have not ruptured and released the fluids this should be done to reduce the size and weight of the uterus. Depending on the position and posture of the fetus and the direction of the torsion, the left or right arm is used for manually rotating the fetus. The leg of the fetus is grasped in the metacarpal or metatarsal region and the knee or hock joint flexed. By repelling the fetus and twisting the leg in rotating manner at regular intervals the fetus and uterus are rocked back and forth through an arc of 10 to 12 inches; and then with a sudden strong twist they are lifted and then pushed downward to the side opposite to the direction of the torsion, thereby in many cases relieving the torsion. Some veterinarians pass the hand alongside the body of the fetus, start it rocking and then lift it upward, over, and downward, in a like manner, opposite to the direction of the torsion. This manual technique is easier in the smaller

breeds of cattle with the smaller and lighter calves. It is also easier for the stronger, taller operators.

In the larger breeds of cows when correction of the torsion is not possible by manual rotation of the fetus and uterus the detorsion rod described by DeMott and Roberts,⁹ or a similar instrument such as Erickson's detorsion rod or Cammerer's fork is of great value. Modification of these detorsion rods to permit the tight attachment of obstetrical chains to the handle is desirable. The DeMott detorsion rod is made of 3/8-inch steel rod, 30 inches long, has an eye at either end with 1-1/4 inch inside diameter. After making an 8- or 9-inch loop in a 60-inch obstetrical chain the end of the loop is passed through one eye of the detorsion rod and the rod and loop of chain are carried into the uterus. The free end of the loop is passed around one leg of the fetus and the rod is pushed up to that leg. The other end of the loop, on the opposite side of the eye of the rod, is passed around the other leg. Both ends of the loop around the legs should be placed around the pasterns or just above fetlocks and the free end of the chain drawn tight. If the loops of chain are passed up the leg to the knees or above the knees of the fetus, the hoofs and feet may be forced into or through the uterine wall as the detorsion rod is rotated unless they are carefully held by the operator. A short piece of broom handle or Gibbon's obstetrical handle is then inserted into the eye of the rod and the tightly drawn chain wrapped several times around the handle.

There is another method of applying this instrument, but it is not as safe inasmuch as it may injure the fetal limbs. If, however, the fetus is dead this aspect is unimportant. A loop is made in the long obstetrical chain. It is carried into the uterus and placed around one or preferably both legs of the fetus. The free end of the chain is placed through one eye of the rod and the rod is pushed into the uterus so that the eye fits tightly on the loop around the leg or legs. The chain is drawn tight and the free end of the chain wrapped around the handle.

Before and during rotation of the fetus and uterus, the hand should be inserted into the vagina and uterus to make certain that no portion of the mucous membrane is being pinched by the chain and that the claws of the feet do not engage or rupture the uterine wall. Vaginal examination during the reduction operation is helpful in making certain that the fetus and uterus are being rotated in the proper direction and in determining when the torsion is corrected. When rotating the fetus, repulsion by means of the rod is definitely helpful. In most cases, rocking the fetus and uterus back and forth a few times before starting reduction of the torsion makes the operation easier. Then the handle is rotated slowly in the direction opposite to that of the torsion, and the torsion is

relieved. Rotating a fetus in anterior presentation a quarter of a turn beyond the normal position and then returning the fetus to the normal position will bring the head into the proper posture. If the torsion and stenosis of the birth canal are not severe and both fetal limbs are lying in the vagina, rotation of the fetus and uterus is simplified; but the torsion should not be overlooked.

Other techniques may possibly be used to correct torsion or to assist in the previous procedures. Abdominal ballotment is recommended⁵ and may be of use in aiding manual correction of the torsion through the birth canal, or in rolling the cow. In right torsion an assistant on the right side pushes downwards and inwards in the upper right flank while an assistant on the left side pushes upwards and inwards on the lower left flank. In left torsion the upper left flank and the lower right flank are pushed strongly with the fists. These two assistants push alternately, at intervals of about one second. This causes the uterus to roll back and forth, aiding the operator who is working on the fetus and uterus through the birth canal. When the cow is on her back during the rolling, alternate pressure through the relaxed abdominal walls may aid in reducing the torsion. If the fetus cannot be palpated per vaginam it is very doubtful that rectal palpation and manipulation would be of much value in aiding correction of the torsion. The stimulation of vigorous fetal movement is an aid to correction of early cases of torsion.⁵ If the hand can be passed into the uterus, the eyeballs of the fetus should be pressed firmly. This results in strong reflex movements of the fetus that may aid manual correction of the torsion. A technique that may be useful in correction of torsion when manual correction of the torsion is to be accomplished by rotation of the fetus and uterus through the birth canal or through a laparotomy incision was illustrated.²⁹ One end of a wide board about 8 feet long is placed on the ground under the abdomen and at a right angle to the body of the standing cow. An assistant pushes upward on the other end of the board into the right flank if right torsion is present or into the left flank if left torsion is present. The operator can lift the twisted gravid uterus and fetus from 4 to 6 inches; the board is pushed into the flank and the uterus rests on the board until the operator can get another hold on the uterus or fetus and lift it higher, where pressure upwards and inward on the board again holds it until the process can be repeated. The gravid uterus is thus "walked up" the board until it is in a position to be pushed over and downward, and the torsion corrected. Another old technique, rather crude and not recommended for cows but useful in ewes is that of suspending a ewe's body by her hocks, until only the ewe's shoulders remain on the ground. The gravid uterus rotates more easily into

its normal position when the viscera fall forward. Abdominal ballotment or manual rotation of the fetus through the vagina or rectum, or both, may be necessary to effect correction.

Cesarean section may be indicated in uterine torsion when correction by laparotomy or other means fails; when the cervix is not dilated or only slightly so and it is desired to save the live fetus; when the cervix has undergone a secondary constriction after prolonged dystocia and an emphysematous fetus is present; when uterine rupture has occurred and the fetus is partially in the abdominal cavity; or when torsion of the uterus is suspected in multiparous animals such as the bitch, queen and sow. In these latter species cesarean section should not be delayed. In the ewe and doe as in the cow, cesarean section may be used whenever ordinary means of handling fail or are not indicated. Before performing cesarean section under these complicated conditions the prognosis should be discussed with the owner, as slaughter may be preferable. In the mare, rolling usually results in correction of this condition, although some veterinarians indicate that rolling may be more hazardous for the mare than reduction by a laparotomy incision in the left flank. Manual or instrumental rotation of the fetus might be attempted but is more difficult and dangerous than rolling. The rotation of the uterine horns in the mare in rotated bicornual pregnancy has been discussed under transverse presentations. In severe uterine torsion, especially in the bitch and queen, in which the uterus is severely damaged and necrotic, hysterectomy is indicated and is usually successful if shock or peritonitis do not present severe complications. When hysterectomy is indicated in the cow, the prognosis is very grave. In rare cases in which torsion has become chronic with many adhesions between the involved horn and uterus and the rest of the abdominal viscera, the cow should be slaughtered. In bitches and queens this encapsulated mass containing macerated or mummified fetuses may be removed if necessary.

After the torsion has been corrected by the above methods, with the exception of cesarean section, the fetus may usually be removed by traction after correction has been made of any abnormal posture of its head, neck, or limbs. Before the fetus is removed the uterus should be examined carefully to make certain a rupture, which is usually located transversely in the uterus just cranial to the cervix, has not occurred. In some cases the cervix is not completely dilated. If the fetus is alive, this may be because the stage of parturition has not progressed sufficiently. The treatment indicated in these cases is to administer 20 to 50 units of oxytocin and wait 2 to 4 hours for further dilation or normal parturition to occur.

A slow intravenous drip of the same amount of oxytocin over a period of several hours may produce a more physiological dilation of the cervix. In most cases, however, the cervix is only partially dilated due to an atony or inertia of the cervix and uterus caused by the torsion of the uterus and interference with normal circulation and the fetus is dead. Due to unrelieved dystocia during the period corresponding to the first and second stages of parturition the cervix may partially contract with the fetus still in the uterus. This latter condition is usually observed with a dead fetus and occasionally fetal emphysema is present. The condition of the fetus is an important factor in the decision whether to wait for the cervix to dilate more or to exert moderate, continuous traction with lubrication at once and gradually dilate or, if necessary, even slightly lacerate or incise the cervix, cervicotomy,³⁴ in order to remove the fetus. When the cervix is poorly dilated great traction is not indicated, since it may cause severe cervical laceration or rupture of the uterus especially when the fetus is dead, or dry and emphysematous. Under these circumstances cesarean section, using one of the ventral abdominal laparotomy sites, is indicated.

After the fetus has been removed, the uterus, birth canal, and the cow should be carefully inspected. Rupture of the uterus with peritonitis, internal bleeding due to rupture of the large uterine vessels, retained placenta, septic metritis, and perimetritis are common sequelae to torsion of the uterus. There should be proper treatment or preventive treatment of these complications.

Dystocia due to Abdominal Hernias, such as inguinal hernias in the bitch and rarely in the queen; large ventral hernias in the mare, cow and ewe; and extensive ventral hernias due to rupture of the prepubic tendon in the mare (see Figure 80) and cow, were described in Chapter 5. Dystocia might be possible but would be of great rarity, due to diaphragmatic, umbilical, or perineal hernias. Inguinal hernias causing dystocia must be relieved by a cesarean section; in some neglected cases hysterectomy might be necessary.³ In rupture of the prepubic tendon in the mare, traction should be provided as soon as the first stage of labor is completed. Induction of parturition might be considered. Cows and ewes may give birth normally even with large ventral hernias but aid should be available if it is needed.

Dystocia due to Vagino-Cervical Prolapse is rarely observed in domestic animals. In most cattle affected with vagino-cervical prolapse that carry their fetuses to term, parturition is usually uneventful. Occasionally abortion with a secondary dystocia may be associated with vagino-cervical prolapse. The vagina or cervix might be severely diseased, atonic, edematous, and traumatized

and cause dystocia that might have to be relieved by lubrication and gentle traction. In rare instances vaginocervical prolapse might be severe enough to indicate cesarean section as an aid to relieving the condition. A cesarean might be necessary if cervical stenosis is present, associated with cervical prolapse (see Chapter 5).

Dystocia Due to Stenosis or Obstruction in the Birth Canal

The immediate causes for dystocia due to stenosis or obstruction of the birth canal may be divided into several groups according to the structures affected—the pelvis, the cervix, the vagina, or the vulva.

Dystocia due to Abnormalities or Injuries of the Pelvic Bones resulting in a stenosis or narrowing of the pelvic inlet is seen commonly in domestic animals. In all animals, especially in the cow and sow, the females may be bred too young and the pelvis at the time of parturition be too small and juvenile to allow passage of the fetus. Primiparous animals, especially the cow and sow, may also commonly have dystocia due to a disparity in the size of the maternal pelvis and the size of the fetus even though bred at the proper age, when they have been grown poorly or stunted, usually due to a lack of the necessary nutrients for normal growth, or have suffered chronic disease processes that prevented or retarded normal growth and development. (See Chapters VII and IX.) Dystocia is common in achondroplastic dwarf cattle. In certain breeds of dogs especially the brachycephalic breeds, with a large broad head, dystocia is common due to the relatively small, narrow flattened pelvis. Pelvic fractures and exostoses as a cause for dystocia are uncommon in the large domestic animals but are occasionally seen in bitches and queens that are struck or injured by moving vehicles. Fortunately most females with fractures and exostoses of the pelvis are not bred. Occasionally in the cow, rarely in the mare, a large or sharp bony prominence may be found on the cranial portion of the symphysis pubis. This prominence may project into the pelvic canal and cause lacerations or contusions of the vagina or cervix when traction is applied to the fetus. It is unlikely that an owner would breed any animal affected severely enough to have pelvic deformities.

Correction of this type of dystocia may be overcome in most cases with steady, moderate traction in the proper direction or directions on a well-lubricated fetus. When there is a bony prominence on the cranial part of the symphysis pubis care should be taken not to rupture or lacerate the vagina, cervix, or uterus. In most cases of

severe dystocia due to pelvic stenosis, in which there is a great difference between the size of the fetus and the pelvic diameters cesarean section is indicated. Fetotomy may be indicated only in selected cases. If the head of the fetus cannot enter the pelvic cavity at the same time as the forelimbs in anterior presentation, or if the fetal pelvis is much larger than the maternal pelvic inlet in posterior presentation, cesarean section is indicated. Especially if the dystocia is severe, the fetus is alive, and mutation and forced extraction offer little hope of success, cesarean section is the method most often selected. If in anterior presentation the fetal extractor can with moderate traction draw the thorax through the birth canal, sometimes after amputation of the head and neck, evisceration through a transverse abdominal incision is performed and the impacted fetal pelvis is bisected with a fetatome. This procedure may be simpler and safer than a cesarean operation. Fetotomy through a narrow birth canal is often difficult, prolonged, and usually must be total rather than partial. The newer percutaneous total fetotomy techniques in selected cases may be indicated.^{6,44} The possibility of severe trauma to the birth canal by prolonged fetotomy operations through a small pelvic inlet is great. In severe cases, even those complicated with fetal emphysema, cesarean section may be more desirable and easier for the operator and the cow than a prolonged, difficult fetotomy operation. Pelvic symphysiotomy might be indicated in certain cases in heifers in range areas. In the bitch, queen, sow, and probably the ewe, cesarean section should be resorted to immediately as soon as dystocia develops. With the exception of young animals which have been on a low nutritive plane, or been bred at too young an age, or possibly brachycephalic dogs, these females should not be rebred after dystocia.

Dystocia due to Failure of the Cervix to Dilate is seen occasionally in the cow and the ewe and very rarely in other domestic animals. In England and Australia this condition is spoken of as “ring-womb,” especially in ewes. Failure of cervical dilation is due to a number of causes—cervical induration, primary uterine and cervical inertia, secondary uterine inertia with cervical involution—and in the early stages of normal parturition this condition might be diagnosed erroneously. In ewes this condition has been associated with prepartum prolapse of the vagina lending further credence to the hypothesis that “ring-womb” is of an endocrine etiology.³

The cervix may fail to dilate because of severe fibrous induration or sclerosis of the cervix. This is observed most often in older cows with a history of cervical lacerations and uterine and cervical infections. The incidence of true cervical induration or sclerosis producing

dystocia is rare and this diagnosis should only be made after a careful clinical examination.

In other cases the diagnosis of stenosis or atresia of the cervix may be erroneous, because the animal may not yet have entered the first or second stage of labor. If the animal is left alone for a number of hours cervical dilation will often take place physiologically. In these animals the uterine tone is good, the fetus is alive, the uterine artery is very large and has the typical whirring feeling, the tenacious cervical seal is loosening and the fetal membranes are intact. There have been rare cases in which for some undiagnosed reason the animal began to strain intermittently a day or more prior to parturition. Rabies in cattle, because of the frequent occurrence of tenesmus in this disease, may resemble approaching parturition in a cow in advanced pregnancy.

Stenosis or atresia of the cervix may be associated with dystocia when, in abortion or at term, the cervix does not dilate completely, or relaxation of the cervix fails to take place. This condition is probably caused by hormonal factors that fail to produce a normal relaxation and dilation of the cervix. It is often associated with uterine inertia. This may be due to a failure of the usual or necessary hormones to be secreted or their receptors to develop or possibly more frequently due to disease of the cervix and uterus that renders the cervical and uterine muscles incapable of responding normally to the hormonal stimulus that relaxes the cervix and produces dilation by contraction of the uterine muscles forcing the fetal membranes and fluids, and the fetus into the cervix. The estrogenic hormone, relaxin, and prostaglandins are considered to play important roles in this process by releasing collagenase causing a breakdown of collagen in the cervix and its relaxation (See Chapter VI, Parturition). The exact mechanism requires further study. Failure of the cervix to dilate properly at the time of parturition is associated with or observed in: uterine inertia, uterine torsion, metritis, placentitis, death of the fetus, septic metritis of pregnancy, diffuse peritonitis due to traumatic gastritis, hydrops of the fetal membranes, a terminal condition in severe septic or toxic diseases, mummified fetus, in certain abortions, preparturient paresis, ketosis in ewes, and twin pregnancies in unipara. The history, evidence of uterine inertia, lack of uterine tone, evidence of a diseased fetal membrane or fetus, possible rupture of the fetal membranes and results of attempted treatment will aid in making a diagnosis.

A further condition resulting in a cervical stenosis is involution of the genital tract. In neglected cases of abortion or dystocia, characterized by a dead and usually emphysematous fetus, ruptured membranes, loss of fluid, and a dry birth canal, a stenosis of the cervix may be

observed. It is seen after correction of uterine torsion, a breech presentation or other prolonged type of dystocia, especially one in which no part of the fetus enters the birth canal. As a result there is a contraction or involution of the cervix with the dead fetus still in the uterus. It may be difficult to differentiate this type from failure of the cervix to dilate when uterine disease results in uterine atony and death of the fetus.

The handling of these cases will depend on the cause of the cervical stenosis, the condition of the fetus and uterine contents, and the uterus. In rare cases due to cervical induration and sclerosis the prognosis is guarded and cesarean section is probably indicated if cervical dilation is slight. Dilation of the cervix by mechanical means such as the operator's hands and arms, instruments, a heavy rubber balloon inserted into the cervix and then inflated, or steady, moderate traction on the fetus, will often result in success in selected cases but the cervix may be severely traumatized. Incision of the cervix, vaginal hysterotomy or cervicotomy^{3,34} might be tried through the dorsal and dorso-lateral portions of the cervix. Such an operation is of questionable value and is dangerous and not recommended for valuable breeding animals. In cases in which normal parturition is approaching or the animal is in the first stage of labor no treatment is indicated; often however, veterinarians will give estrogens and oxytocin and wait for normal birth to occur. As described previously in Chapter VI, parturition in mares may be induced more physiologically by 30 to 50 units of oxytocin in saline given by an intravenous drip technique over a period of several hours.

In the type of case in which the cervix fails to dilate due to uterine inertia, diseased uteri, metabolic diseases, and others, the prognosis is guarded and a careful diagnosis should be made if possible. If sufficient time is available a large dose of estradiol, 20 to 30 mg. and/or 20 mg. of dexamethasone administered intramuscularly possibly with prostaglandin F_{2a} , and repeated every other day if necessary, may aid relaxation of the cervix and initiation of parturition. Injections of oxytocin and calcium gluconate may improve the tonus of the uterus and aid or hasten cervical dilation. Uterine relaxants and spasmolytics have been used in other countries.³⁴ Gradual traction on the fetus along with lubrication massage and stretching of the cervix of the cow may relax the partially dilated cervix sufficiently after one-half to one hour to remove the fetus. Strong, forced traction on the fetus is to be avoided, since it pulls the stenosed cervix caudally toward the vulva, narrowing its lumen. Strong traction may cause a transverse rupture of the uterine wall just cranial to the cervix. Occasionally, however, forced extraction, even though it produces a slight to

moderate laceration of the cervix, is indicated over fetotomy or cesarean.

Good lubrication is essential. Fetotomy is very difficult because of the small diameter of the cervix. Cesarean section may be indicated especially if the fetus is alive and the uterus free of infection. In cases of parturient paresis occurring during parturition, an intravenous injection of 250 to 750 cc. of a 20 percent solution of calcium gluconate usually results in parturition within 4 to 6 hours. In ketosis in ewes the fetuses are usually dead and the ewe will die unless the fetuses are aborted and removed promptly; cesarean section therefore may be necessary.

In neglected dystocia cases with cervical stenosis due to involution of the cervix, the prognosis is poor because the fetus is usually emphysematous. The uterus may already be ruptured or may easily be ruptured if forced extraction is applied. Fetotomy, moderate careful forced extraction with much lubrication, or cesarean section, may be attempted depending upon the conditions and the judgment of the operator. Following the correction of the dystocia, the aftercare of the animal is important, as septic metritis, retained placenta, perimetritis, necrotic vaginitis, metritis, and cervicitis are common. In the bitch and queen cesarean section or hysterectomy are usually performed in cases where there are conditions associated with uterine inertia.

Dystocia due to Stenosis or Obstruction of the Vagina may be found in all species. It may be due to tumors such as fibromas or leiomyomas. In rare instances in the mare, ewe, sow or cow dystocia may be due to compression of the vagina by a massive intrapelvic hematoma often following rough intervention by laymen. This may develop during forced extraction or a fetotomy operation. In rare cases a pelvic abscess, excessive fat around the vagina, or possibly a perineal hernia may cause dystocia because of compression of the vagina. A high incidence of fat necrosis was reported in beef cattle grazing on heavily fertilized fescue pastures in northern Georgia.³⁹ In some cattle the fat necrosis was extensive enough to cause a stenosis of the birth canal. In occasional instances a severe necrotic vaginitis may heal and the resulting scar tissue cause a marked stenosis of the vagina and dystocia at the next parturition. A persistent hymenal band may cause stenosis of the birth canal. A persistent median wall of the Mullerian duct, usually found as a fibrous band from 0.5 to 2 inches in diameter just caudal to the cervix, may cause dystocia if the limbs of the fetus straddle this band. This condition is seen most commonly in the cow but may rarely occur in other species.¹³ Either rearing the heifer under unfavorable conditions, or breeding the heifer at too young an age, may cause dystocia due to vaginal infantilism. Occasionally,

however, in abortions or premature births in heifers, the normal relaxation of the birth canal does not occur and dystocia results, due in many instances to lack of normal dilation of the cervix and vulva rather than to underdevelopment of the vagina.

The handling of vaginal stenosis will vary with the cause. If a tumor is present it often can be repelled cranial and lateral to the pelvic inlet as the fetus is withdrawn. In dystocia due to a persistent wall of the Mullerian duct, the fibrous band can be located and cut with a knife or scissors. In mild cases of vaginal stenosis steady moderate traction on the fetus, together with good lubrication, will usually dilate the vagina and allow the fetus to be removed. Occasionally if excessive traction is applied, rupture of the vagina may occur with prolapse of fat or the bladder. In most severe cases of vaginal stenosis, obstruction, or compression, especially in multipara, cesarean section is the method of choice for relief of dystocia. Fetotomy is of very limited or no value because the small size of the vagina makes manipulations and operations very difficult and conducive to postpartum necrotic vaginitis.

Dystocia due to Stenosis or Constriction of the Vulva and Vestibule is occasionally seen in the heifer or mare and less commonly in the other animals. It is usually observed in heifers with genital hypoplasia due to improper growth of the heifer because of chronic disease or poor nutrition or due to a genetic recessive such as anovestibular stenosis or rectovaginal constriction (RVC) in Jerseys.²⁰ Dystocia due to a small vulva may be observed sometimes in heifers that abort or calve prematurely before the vulva is properly relaxed. About 55 percent of dystocias in two-year-old Angus heifers was due to stenosis of the vulva or vestibule.²⁸ This incidence seems too high unless mild stenosis predominated or the heifers were too fat. In exceptional instances it may be hereditary in nature or be secondary to extensive scarring from lacerations following previous parturitions or dystocias. In anterior presentation the nose and head, and in posterior presentation the thighs or stifles stall at the vulva or vestibule. This condition will also occur when large mummified fetuses are expelled by injections of prostaglandins because the genital tracts are not relaxed by estrogens or relaxin.

The treatment or handling of stenosis of the vulva is best performed by gradual, steady, moderate traction over a period of 1/4 to 2 hours, in order to dilate the vulva slowly. The use of lubrication is essential. Prolonged attempts to dilate the vulva, especially if care and lubrication are not used, may result in an extensive necrosis and cellulitis of the vulvar and vestibular tissues. Stretching the vulva by pulling it over the fetal head and pushing outward on the vulva from the inside with the

hands and wrists, helps to dilate it. Moderate traction on the fetal head alone, with the feet released, will help draw the head through the vestibule and aid dilation because of the triangular- or wedge-shape of the fetal head. Patience is essential, since excessive or too-rapid traction will rupture the vulva, vestibule or perineum, causing laceration, severe hemorrhage or contusions. Excessive traction on the fetal jaw may fracture it. Excessive rotation of the fetal head should be avoided. Placing the hand over the poll and pulling the head ventrally and caudally and the vulva cranially and dorsally helps slide the dorsal commissure of the vulva over the top of the fetal head. Severe laceration of the vestibule and vulva rarely occurs, even in the mare, when parturition proceeds unassisted; but if traction is applied, even by one man, laceration may be severe because normal, gradual dilation was not permitted.

If the vulva and vestibule fail to dilate within a reasonable length of time, if haste is imperative or if it is obvious that vulval dilation will not occur, an episiotomy may be performed under epidural anesthesia or local infiltration of the incision sites.^{12,34} With the vulva under tension an incision should be made on either side of the dorsal commissure in a dorso-lateral direction. This is done to prevent a recto-vaginal laceration or a "gill flirter" in the larger domestic animals, in which the dorsal commissure of the vulva is near the rectum. In multipara the vulva is a greater distance from the rectum and an episiotomy is made in a dorsal direction toward the rectum. After removal of the fetus the episiotomy incisions should be sutured together immediately with interrupted deep vertical mattress sutures of catgut and/or nylon and the animal treated with antibiotics for several days.

Fetotomy is not indicated in these cases for the same reasons as in vaginal or pelvic stenoses. In rare cases cesarean section may be the method of choice particularly in multiparous animals or if the live fetus is to be saved. Gradual, moderate traction is the most satisfactory method, inasmuch as dilation of the vulva is necessary or advisable in order that the dam may give birth without assistance at subsequent pregnancies.⁴²

In mares and cows in which the vulva has been sutured to prevent pneumovagina, this band of tissue should be cut just before parturition in order to prevent uneven or irregular tearing of the scar between the two vulvar lips. This thin band of tissue will not cause dystocia.

Dystocia Due to Uterine Inertia

For convenience in discussing this problem it will be divided into two parts: primary inertia and secondary in-

ertia. Both are characterized by a weakness or absence of uterine contractions during the first or second stage of labor that usually persists into the third and involution stage after parturition.

Dystocia due to Primary Uterine Inertia is observed most frequently in the bitch, cow—especially the older dairy cow—and sow. It is uncommon in the other species. It is produced by a lack of tone or failure of the uterine muscles to contract. The failure of the uterine muscles to contract normally at parturition may be due to a primary failure of the muscles to respond to hormonal stimuli due to disease of the muscle; or it may be due to an actual lack or failure of release of hormones or the development of receptors such as estrogen, oxytocin and possibly prostaglandins that initiate uterine contractions in normal muscles (See Chapter VI, Parturition). In bitches it is observed more frequently in certain small breeds such as the Dachshund. In a few Cocker spaniels it may be associated with psychotic abnormalities and nervous voluntary inhibition of parturition due to pain. Primary uterine inertia was common in infertile dogs with 3 or fewer fetuses.^{3,11} Lack of exercise, excessive fatness, debility, and senility are all causes of weakness of uterine contractions at parturition. Overdistension of the uterus in fetal giantism, hydrops of the fetal membranes, fetal anasarca, twins in unipara—especially unicornual twins—and an excessive number of fetuses in small bitches are other conditions conducive to primary uterine inertia. Undoubtedly uterine disease, or pathology associated with uterine infections and placentitis during gestation, also play a role in the production of uterine inertia. Apparent bovine uterine inertia is observed in parturient paresis due to a hypocalcemia. A type of primary uterine inertia in dogs, especially Chows, Retrievers, Bull Terriers and Spaniels, associated with a small litter, with slight or absent mammary development, and with no signs of parturition at the proper time has been described.⁵ The fetuses apparently succumb and by 70 to 80 days after service a dark green viscid fluid escapes from the vulva. This was probably due to a hormone disfunction.

The animals affected with primary uterine inertia are usually and obviously parturient and in the first stages of labor, as shown by relaxation of the soft structures of the pelvis, marked mammary development, and discharge of mucous from the vulva. The animals show no distress and eat and drink nearly normally but the second stage of labor does not occur for 6 to 36 hours or more, if at all. On examination, the cervix is usually relaxed and dilatable but the fetus and fetal membranes are not being forced into the cervix or birth passage. In some cases in cattle the cervix fails to dilate normally due to a lack of hormones or to a failure of the uterus to con-

tract. What may be diagnosed as a failure of the cervix to dilate may in reality be a manifestation of a primary uterine inertia. One or both membranes may have ruptured. There is usually no abnormality in presentation, position, or posture of the fetus. The uterus apparently fails to contract normally, and consequently does not force its contents through the cervix and into the birth canal. Usually in 24 to 48 hours the second stage of labor may set in but in many cases by then the fetus is dead and occasionally infection of the fetal membranes and fetus is apparent. The prognosis is favorable in most cases that are diagnosed early.

In the cow or ewe this condition is rather easily handled if the cervix is relaxed and open by rupturing the membranes, correcting any abnormal posture, and removing the fetus by moderate or slight traction. In certain cases in the cow as well as in multiparous animals in which the condition is diagnosed early, intramuscular injections of oxytocin, 2 to 10 ml (20 to 80 units) for large animals, or 1 to 2 ml (10 to 20 units) for small animals, may stimulate uterine contractions and normal birth of the young. Giving this injection in saline by an intravenous drip technique over a period of several hours may be a more physiologic procedure. Others state that the intravenous injection of calcium gluconate, 500 ml of a 20 percent solution in cattle and 10 ml of a 10 percent solution in bitches, is of value in these cases, especially if calcium levels of the blood are low or if parturient paresis is present. In the bitch as well as other species "feathering" the vagina by inserting a finger, and stroking the dorsal wall of the vagina, or in other similar ways stimulating the production of oxytocin by the animal's own pituitary may be helpful. If this treatment does not result in the initiation of normal parturition in 1 to 2 hours the treatment might be repeated. After 3 to 4 hours with no response, cesarean section is indicated and should be performed at once in the multiparous animals. If according to the history primary uterine inertia has existed for 4 to 6 hours before the veterinarian examines the case, cesarean section may be indicated at once rather than the use of the above techniques and waiting for uterine contractions to begin. Hysterectomy may be preferred if evidence of infection is present in the uterus of the bitch or queen. Morphine, 1/8 to 1/2 grain or tranquilizers may quiet nervous, psychotic Cockeris sufficiently to permit normal parturition.

Since this inertia extends into the third stage of parturition and beyond, retained placenta, metritis, and delayed involution of the uterus are common. Administration of several injections of oxytocin or ergonovine accompanied by intrauterine and parental antibiotic therapy, may help prevent septic metritis and other compli-

cations due to delayed involution of the uterus.

Secondary Uterine Inertia usually follows a prolonged dystocia and is characterized by exhaustion of the uterine muscle. This condition is seen in all species and is more common in large animals than is primary uterine inertia. In multiparous animals when prolonged labor or dystocia is relieved by removing the fetus causing the dystocia, it is quite common to find that secondary uterine inertia has occurred and consequently the rest of the fetuses are not expelled. This type of inertia can be prevented by correcting dystocias early. In certain breeds of dogs such as the Scotch Terrier or Dachshund secondary uterine inertia may occur spontaneously early in the second stage of parturition. Usually one or two fetuses are expelled normally and then labor ceases even though more fetuses are present in the uterus.

In cattle examined after prolonged dystocia the uterus is often contracted tightly around the fetus. In some cases this condition closely resembles the condition called retraction, Bandl's, or contraction ring dystocia, described in humans following prolonged dystocia.²⁷ In retraction ring dystocia the uterine muscle just cranial to the cervix contracts tightly, so that normal expulsion of the fetus into the birth canal can not take place. A contraction ring may occur any place in the uterus and if it occurs around the fetus it can interfere with birth. These abnormal contractions of the uterine muscle are strong sustained tetanic contractions caused by exhaustion spasms of the muscle which are a fatigue phenomena. Diagnosis of this condition may be based on the history of prolonged dystocia; in multipara on the birth of one or two fetuses with a cessation of labor, or the removal of the fetus causing the dystocia, not followed by the normal resumption of parturition. In large animals intrauterine examination reveals the nature of the condition causing the dystocia—usually an abnormal position, posture, or presentation, and the contraction of the uterine walls upon the fetus. In some uteri in which contraction bands or rings are very strong and broad especially around or caudal to the fetus, this condition will complicate the primary cause for the dystocia. The prognosis in secondary uterine inertia is more guarded than in primary uterine inertia because the fetuses may be weak, dead, or emphysematous, and rupture of the uterus is more common. Retained placenta and metritis are usual sequelae.

In the handling or correction of this type of dystocia in large animals the condition causing the original dystocia should be corrected by mutation if possible and the fetus then removed by moderate, careful traction. Lubrication of the fetus and birth canal is usually necessary. Excessive traction should be avoided if strong contraction or retraction rings are present in the uterus and

definitely retard removal of the fetus, since transverse rupture of the uterus may occur. This is a highly important reason for examining the uterus carefully in prolonged dystocia cases as occasionally ruptures occur spontaneously or due to previously applied traction. If contraction rings are not too strong, careful, slow, cautious mutation and traction may be successful in relieving the dystocia. If they are severe and markedly reduce the lumen or diameter of the uterus it may be necessary to resort to fetotomy or cesarean section to relieve the condition. In other countries uterine relaxants or spasmolytic or tocolytic drugs, such as isoxsuprine lactate, are recommended in this condition.^{3,25,34} Since infection of the uterus is often present, the ventral abdominal approach for the cesarean operation is indicated. In humans these contraction or retraction rings may be relaxed by intravenous administration of adrenalin or modern relaxants and by general anesthesia; if this fails, a cesarean is necessary. The author in a limited number of bovine cases has had little success using adrenalin. Epidural anesthesia is not effective in relaxing the uterine muscle. In bitches, mild narcosis or anesthesia with morphine may be helpful. This marked contraction of the uterine wall in prolonged gestation is another reason for being very careful not to rupture the uterus by repelling the fetus in an attempt to gain room for mutation operations.

In the sow it is common practice, when several pigs have been expelled before dystocia occurred, to remove by traction the one causing dystocia, lubricate the birth canal, and give 1 to 2 ml. of oxytocin, or 2 to 3 ml. of **Lentin**. If the rest of the litter is not expelled in 2 to 3 hours, another pig may be removed by traction and the injection repeated; or cesarean section may be decided upon as the method of choice. This decision should not be delayed too long. In bitches the situation is similar to that in sows, in that the handling of the case will depend upon the duration of labor, the number and condition of the fetuses, and the degree of uterine infection. Early cases in bitches may be handled in the same manner as in sows except that **Lentin** should not be used. If the dog appears exhausted but the fetuses are in good condition, 1/4 grain of morphine will relax the bitch and possibly the uterus and after one or two hours rest strong uterine contractions will commence again and whelping continue. In this condition of secondary uterine inertia, helping the bitch with forceps may be indicated if only one or two fetuses remain in the uterus. If, however, there are 3 or more fetuses and dystocia has been prolonged, cesarean section is indicated. If the fetuses are dead and infected, hysterectomy may be desirable. Cats are quite resistant to infection. Oxytocin usually will reinitiate labor even after dystocia of 48 hours' dura-

tion.³² As in primary inertia, retained placenta, septic metritis, delayed involution, and pyometra are common following secondary uterine inertia.

Dystocia Due to Postmortum Changes in the Fetus

These dystocias may be caused by mummification of the fetus in cattle, and by fetal emphysema and fetal maceration in all species.

Dystocia due to Fetal Mummification in cattle was described in Chapter 5. In some instances mummified fetuses may macerate. This is probably secondary to a relaxation of the cervix at the time of an unobserved, spontaneous, but incomplete abortion. Organisms entered the previously sterile uterus and start the maceration process. Hematogenous uterine infection may possibly occur.

Dystocia due to Fetal Emphysema is observed in all species and is usually associated with a prolonged dystocia of 24 to 48 hours' duration. The fetus dies and organisms from the vagina pass through the open cervix, invade the uterus and cause rapid fetal emphysema. Fetal emphysema may complicate dystocia in incomplete abortions after the fourth month of pregnancy when the dead fetus is retained in the uterus (see Chapter 5). Although fetal emphysema usually occurs with the cervix open it may occur with a closed cervix in rare conditions such as a septic metritis of pregnancy in which the fetus dies, becomes emphysematous, and may even macerate before the cervix opens. Such a condition occurring late in pregnancy especially in a heifer with a small, underdeveloped, or unrelaxed genital tract may result in a serious and often fatal termination. Fetal emphysema is also observed in cases of neglected torsion of the uterus in which the fetus dies. It is commonly seen in rotated bicornual pregnancies in mares. In any type of condition causing uterine inertia, fetal death and emphysema may result if treatment is not given promptly. In bovine twin pregnancy one twin may be expelled and the other remain in the uterus and become emphysematous or macerate. This is more commonly seen in unicornual twins. Dystocia due to any condition causing the death of the fetus may result in fetal emphysema if the fetus is not removed promptly. In bitches and sows fetal emphysema may occur in prolonged dystocia in a manner similar to that in other animals. It is also observed in the large breeds of dogs such as Great Danes, Afghans, Boxers, Newfoundlands, and St. Bernards. In these dogs birth proceeds normally until the last fetus.⁵ This remains in the uterus and goes undetected for one or two days; by

at this time the bitch shows a fever of 103°, there is a green, black, fetid discharge from the vulva, the bitch manifests no interest in the live pups, and exhibits symptoms of depression and toxemia. In these breeds a careful examination should be made for the last fetus, if necessary by radiographs of the bitch, since usually this last fetus cannot be palpated through the abdominal wall or felt by forceps through the birth canal.

Fetal emphysema can usually be suspected if dystocia has existed 24 hours or more. The animal is usually depressed, toxic, and shows anorexia. Labor is usually weak and intermittent. The temperature is frequently elevated early but may be normal or subnormal late in the condition or at the time the veterinarian is summoned. This is especially true in the cow. The heart and respiratory rates are elevated. The extremities are cold and the feces may be loose and fetid. Often a fetid, watery, reddish vaginal discharge is observed. The mucous membranes of the genital tract are dry, swollen, and inflamed. In some cases the cervix may be partly involuted or contracted. The uterine walls are contracted closely about the fetus. The fetus is dead and swollen because of gas, that can be felt as it crepitates beneath the skin. In early cases of fetal emphysema only that portion of the fetus nearest the vulva may be emphysematous, but in prolonged dystocia cases the entire fetus is involved. In some cases of twins, the twin nearer the cervix may be emphysematous and the deeper twin may be normal. The fetal hair may be beginning to shed. Fetal meconium is often present on the fetus. The corneas of the eyes are grey; and the teeth usually loose. Rupture of the uterus may be present or be easily produced by traction due to the dry fetus and the tense, contracted uterine walls. Examination is likely to result in violent straining. The prognosis is always guarded to poor as uterine disease, septic metritis, and retained placenta usually follow this condition. The future breeding life of the dam is in doubt. Complications such as rupture of the uterus are likely to arise in the handling of dystocia due to fetal emphysema, making the prognosis guarded to grave.

The least difficult and the best method of correction of fetal emphysema in large animals is forced extraction after mutation, if the latter is necessary. Care should be used in repelling the fetus and in exerting traction of the fetus, so that rupture of the uterus or cervix does not occur. Lubrication of the birth canal and fetus is essential. In bitches forced extraction is probably not indicated unless only the one fetus is present or is wedged in the birth canal so that it would have to be removed by traction before a hysterotomy or hysterectomy is performed. In some cases such a fetus may be pulled apart and a portion may drop back into the uterus and become

difficult to remove by forceps. Occasionally in large animals fetotomy may be necessary. Extensive mutilation of the fetus and its evisceration greatly reduce the size of the fetus by releasing the gases present. The fetal tissues are soft and friable due to the emphysema and operations are performed with greater ease and speed than in normal fetuses if the birth canal is dilated. Frequent lubrication is essential to prevent trauma to the birth canal. Necrotic vaginitis or vulvitis or even metritis are likely to follow removal of an emphysematous fetus. In large animals cesarean section is indicated when the birth canal is involuting and is small, swollen, and dry, and when the uterine wall closely invests a greatly swollen and emphysematous fetus. If the cow's life is to be saved a cesarean may be a last resort if fetotomy is not feasible or possible. A total fetotomy of an emphysematous fetus may be more exhausting and dangerous for the cow and operator than is a cesarean section. The prognosis should be guarded and the operation performed on the ventral abdominal wall so that contamination of the abdominal cavity can be avoided. In removing emphysematous fetuses in uniparous animals care should be taken not to leave a hoof in the uterus that might remain and act as a chronic foreign body, producing chronic pyometra.

Another possible technique for relief of dystocia due to bovine emphysematous fetus is to make a long laparotomy incision in the left flank, suture the uterus to the peritoneal and fascial tissues around the periphery of the incision. The uterine wall is incised and sutured with non-absorbable material to the musculature and skin. The fetus and membranes are then removed, by fetotomy if necessary, thus preventing contamination of the peritoneal cavity. The vaginal and uterine cavities are well irrigated and parenteral antibiotics administered. The cow may be slaughtered for beef several months later.³⁸

In the bitch and other multiparous animals cesarean section may be indicated. Many veterinarians prefer to perform a hysterectomy in dogs and cats in order to prevent possible contamination of the abdominal cavity. In multipara with emphysematous fetuses, secondary uterine inertia, or associated uterine torsion, administration of oxytocin might result in uterine rupture and death due to peritonitis and shock. In these cases care should be taken to prevent shock and hemorrhage and to be certain a fetus is not left in the birth canal.

The aftercare of cases of dystocia due to fetal emphysema should consist of antibiotics parenterally and into the uterus, and injections of oxytocin and ergonovine to stimulate uterine contractions, an increased blood supply to the uterus, and to hasten the overcoming of infection. Other supportive therapy such as blood, saline, and glucose may be given, inasmuch as septic metritis and re-

tained placenta are common sequelae to the removal of an emphysematous fetus.

Fetal Maceration as a Cause of Dystocia in incomplete abortions was discussed in Chapter 5. It may develop in all species during pregnancy, as a sequela to abortion or mummified fetuses that were not expelled when the cervix dilated. In rare cases this condition may be observed following undiagnosed and untreated torsions of the uterus during pregnancy or at term. In all animals the uterus or a twisted segment of it containing the macerating fetuses may be walled off in the abdominal cavity; or if the uterus ruptures and the fetuses escape into the abdomen, they may become walled off there and macerate. In rare cases some fetuses may slough to the outside or into the alimentary tract. In uniparous animals uterine torsion can cause fetal death and maceration with adhesions between the uterus and the other abdominal viscera. Fetal maceration is often observed in animals at term when a dystocia or a twin fetus has been overlooked or neglected for 3 to 10 days.

The symptoms are usually limited to a persistent, fetid, vaginal or vulvar discharge often containing hair, hooves, or bones. The cervix is usually partially dilated and the fetus is in an advanced stage of emphysema, maceration and decomposition and pulls apart when handled. In chronic cases the cervix is only slightly open, and the animal fails to show estrus. On rectal examination fetal bones can be felt to crepitate within the uterus. In some cases a perimetritis may be present. In undiagnosed or untreated dystocias a history of constant but intermittent straining, generally considered by the owner as due to retention of the placenta, is noted, as is also a fetid, purulent discharge. The lack of general symptoms shown in some of these cases is amazing. The author observed a 7-year-old cow with macerating twins in the uterus. The owner believed the cow had calved 7 days before on pasture, although he had found no calf. The cow was eating normally and milking 30 lbs. a day. The fetuses were pulled apart in removal through the cervix, which was about 12 cm. in diameter. The uterine wall was about 3 to 5 cm. thick. Recovery was uneventful. A number of similar cases have been described in mares that subsequently conceived following the removal of the macerating fetus.²⁴ The fact that other veterinarians have similar experiences suggests that in extremely difficult dystocia cases it might possibly be advisable in certain cases to try only supportive treatment and antibiotics, for 4 to 6 days, until the fetus has macerated sufficiently to be removed easily. During this same period the uterine wall builds up its natural defenses against infection. The dangers might be uterine rupture due to fetal emphysema before the inception of

maceration or further closure of the cervix which might be prevented by injections of estrogens. In certain cases exploratory laparotomy may be advisable. The prognosis in these cases, occurring more than three days to a week following dystocia, is guarded. In the more chronic cases, with the cervix nearly completely closed the prognosis is very poor.

When these cases in large animals occur, they are handled in a manner similar to that of treating emphysematous fetuses. In the more chronic bovine cases the cervix cannot be dilated manually. Estrogens are usually ineffective in evacuating the uterus, as the bones are more or less imbedded or caught in the endometrium. Laparohysterotomy or hysterectomy in the cow is very difficult in chronic cases with only fetal bones and pus in the uterus because the uterus is so small it is difficult to bring to the abdominal incision even if no adhesions were present. The prognosis as far as the future breeding life is concerned is very poor. Since most of these animals are in fair to good health, slaughter is usually advised. In multipara, especially bitches, hysterectomy is advised in most cases.

After handling cases of fetal emphysema or maceration in large animals, especially if fetotomy was performed, the operator should be careful to cleanse and disinfect his arms and instruments carefully, and then boil the instruments. This is done to avoid a severe infection on the arms or the introduction of infection into the next cow through the use of the contaminated instruments. Aftercare of cases of fetal maceration in which the fetuses were removed is similar to that following fetal emphysema.

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Chapter XI

INJURIES AND DISEASES OF THE PUERPERAL PERIOD

The injuries and diseases of the puerperal period discussed in this chapter include puerperal infections and metabolic diseases as well as hemorrhages, lacerations, contusions, ruptures, and prolapses of various organs, especially the genital organs that may occur during or following parturition. A summary of the causes of post-parturient paraplegia is included. In a study of 2,480 cases of dystocia⁴³ in six dairy and four beef breeds reported by veterinarians in Australia in 13 country practices, a total of 528 dams, 21.3 percent, suffered parturient or post-parturient conditions with about one-quarter of the dams being affected with two or more complications. A partial list of the complications and their incidence were: paraplegia other than hypocalcemia 9.1 percent; retained placenta, 4.9 percent; septicemia and toxemia, 2.7 percent; injury to vagina and cervix, 2.2 percent; uterine rupture 1.0 percent; metritis, 1.1 percent; peritonitis, 1.0 percent; lameness and paresis, 0.9 percent; shock, 0.8 percent; prolapse of portions of birth canal, 0.6 percent and hemorrhage 0.3 percent. Maternal death was usually associated with a prior existing disease state or developed as a result of it and aggravated the dam's condition.⁴³

Postpartum Hemorrhages

Hemorrhage or bleeding into the uterus or birth canal may occur postpartum due to trauma, lacerations, or rupture of the genital organs. Hemorrhage into the uterus may be due to bleeding from an incised or torn caruncle or caruncular stalk in the cow or ewe, from the incised or lacerated endometrium in the mare, or from premature removal of the fetal membranes or placenta. This accident may occur at the time of parturition, during a cesarean section or fetotomy, or may take place later due to improper or too early removal of a retained placenta in any uniparous animal. Severe intrauterine hemorrhage in rare cases occurring from several hours to a day or so after calving and dropping of the placenta, that resulted in a massive blood clot filling the gravid horn of the uterus was described.^{59,60} Rarely death may occur. Slight bleeding may be observed, from the rup-

tured end of the umbilical cord or from slight lacerations of the uterus, cervix, vagina, or vulva. A hemorrhagic discharge from the vulva in a bitch was due to an invagination of a portion of one horn not visible externally.³⁰ In severe lacerations or rupture—particularly of the cervix, vagina, and in rare instances, the vulva—hemorrhage may be profuse due to a rupture of a large vessel. Blood may flow in a stream from the vulva as soon as the fetus is removed. Most of these lacerations and injuries follow forced extraction. Intraperitoneal or extravaginal hemorrhage may occur. If severe enough the former may produce acute symptoms of anemia and rarely death, especially in the mare. This is ordinarily seen in cases of dystocia, rupture of the uterus and uterine vessels before, during, or after correction of torsion of the uterus, in prolapse of the uterus, and in trauma especially in fetotomy operations or forced extraction in young heifers. These hemorrhagic conditions would be greatly aggravated in cattle fed moldy sweet clover hay.

In the treatment or handling of these conditions the usual surgical procedures to control the hemorrhage and supportive treatment are indicated. Most cases of slight bleeding from the genital tract at parturition are not serious and require no treatment. In more severe bleeding from the uterus of large animals oxytocin, 20 to 50 I.U., may help control hemorrhage by contracting the uterus and its vessels. Injecting 500 ml. of saline to which 10 cc. of formalin has been added, or 500 ml. of calcium gluconate may also aid in hastening the clotting of blood, and thus control the hemorrhage. If bleeding occurs from a large vessel through a laceration in the vaginal wall, the vessel may be clamped by forceps. These should be left in place for 24 to 48 hours, or the vessel should be ligated. If this cannot be accomplished, packing the vagina to provide intravaginal pressure should be done promptly. In severe intrauterine hemorrhage the clot should not be disturbed. In several weeks or months the large clot will be reduced and absorbed by natural processes. Intrapelvic or perivaginal bleeding may cause a stenosis of the vagina during or after forced extraction or fetotomy but neither it nor the intrauterine hemorrhage is usually fatal. In 12- to 21-year-old mares rupture of the uterine vessels and sudden death due to hem-

orrhagic shock may occur before, during or after an apparently normal gestation and parturition. The middle uterine artery was most commonly involved but the iliac or utero-ovarian arteries occasionally were affected. Prepartum rupture occurred most often in the latter vessel.⁴¹ Most fatal hemorrhages occur intraperitoneally due to rupture of the large vessels in the broad ligament caused by degenerative changes in the vessel wall, especially in mares or by torsion of the uterus or prolapse of the uterus. Definite symptoms of severe hemorrhage may be observed, indicated by weakness, depression, very rapid pulse and respiration rates, and pale mucous membranes and death within a few hours.³⁴ If the operator promptly enters the peritoneal cavity through the abdominal wall in the flank region or through the uterine wall in prolapse, he may be able to control bleeding by ligating the ruptured vessels. The prognosis is very poor in these cases as severe hemorrhage, shock, and death may occur in rapid succession. In mares early signs of colic, sweating, pain, rapid pulse rate and moderate anemia may occur due to rupture of a uterine vessel with relatively slow loss of blood between the two layers of the broad ligament causing a large hematoma. If this ruptures intraperitoneally within the next few weeks then severe acute signs of shock, rapid weak pulse, anemia, prostration and death follow. If hemorrhage is severe enough to cause clinical symptoms, blood transfusions of 2,000 to 8,000 ml. or more in large animals, saline injections, gelatin or other types of solutions designed to maintain blood pressure should be given, and repeated as often as necessary. The mare should be sedated with a large dose of a tranquilizer and closely confined.

In lacerations or ruptures of the genital tract preventive treatments to control infection should be used, such as the administration of sulfonamides, antibiotics, or local mild antiseptics. Thrombosis of the larger uterine arteries and veins is occasionally observed or described in animals. Thrombi are seen most often in the veins following prolapse of the uterus or uterine torsion when circulation has been restricted. Occasionally an aneurism of the middle uterine artery may be palpated on rectal examination after parturition in the cow, or a hematoma in the broad ligament of the mare. Adhesions between the genital tract and ovaries and other pelvic and abdominal organs and tissues may occur following postpartum hemorrhage.

Subinvolution of the placental sites formerly called "persistent decidual reaction" and occasionally mistakenly called uterine chorioepithelioma is observed infrequently in bitches and is characterized by a persistent discharge of blood from the vulva for 30 to 60 or more days after whelping.^{2,6,31} Subinvolution of the placental

sites should be differentiated from cystitis, uterine tumors, acute or chronic metritis, and cystic endometrial hyperplasia. This condition has been reported¹¹ in Alaskan Malamutes and in some cases causes a decline in the hematocrit. The bloody discharge was nonfetid and it ceased about two weeks before true estrus. Conception occurred normally.

Normal involution of the canine uterus requires about 12 weeks. In a study of 95 postpartum bitches' uteri 20 had subinvolution of one or more placental sites indicating that hormonal influences or infection were probably not causative factors.² The lesions of subinvolution of certain placental sites include sites that are twice normal size and hemorrhagic and on microscopic section several large collagen masses, dilated endometrial glands, and numerous "trophoblast-like (decidual) cells," are usually seen.^{2,6,31} In the normal bitch these latter cells regress and disappear spontaneously within a month postpartum. The pathogenesis of subinvolution is unknown. Further studies are indicated. The discharge of blood in affected bitches is most noticeable about the time of weaning. Most bitches recover spontaneously without or despite various treatments including progesterone.^{4,31} Occasionally a few bitches become anemic and ovariectomy and blood transfusions may be necessary.^{2,29} Most recovered bitches subsequently breed and whelp normally.

Lacerations and Contusions of the Birth Canal and Adjacent Structures

After each dystocia operation the operator should carefully examine the uterus and genital canal for evidence of contusions and lacerations. Minor lacerations and trauma are common especially to the vulva, vestibule and cervix in uniparous animals after forced extraction or fetotomy. Since the vagina is freely dilatable it is less often injured. Minor lacerations are of little importance and usually heal promptly without treatment. Although the more severe lacerations of the cervix in cows seldom result in rupture, a few veterinarians recommended that these be immediately sutured through the vagina to prevent the healed cervix from gaping or being ectopic, and to prevent the formation of excessive connective tissue in the cervix. Mild lacerations of the endometrium heal promptly. These may be aided to heal by the injection of oxytocin which favors uterine contraction. Vaginal lacerations generally occur near the vulvovaginal border. Lacerations of the vulva are usually mild when parturition is normal. Occasionally the mare, especially if sutured by the Caslick operation, will

tear the vulva in a normal parturition. In the mare and cow vulvar and vestibular lacerations are quite common when strong traction is applied too rapidly to permit normal dilation of the vulva. Mild lacerations need not be sutured. Deep lacerations or episiotomy incisions should be promptly sutured after parturition with deep vertical mattress nylon or catgut sutures to prevent gaping and scarring of the vulva and thereby predisposing to vulvitis and vaginitis. Parenteral antibiotics should be administered. Certain mares and cows with relaxed, flaccid, tipped or horizontal vulvas should have the dorsal half or two-thirds of the commissure sutured as described under the Caslick or vulva-suturing operation to control postpartum infection. Lacerations, if not sutured, commonly become infected especially if the tissue is traumatized or devitalized or if metritis and retention of the fetal membranes are present. Infected lacerations of the vulva and vestibule result in pain, swelling, and persistent straining or "wind sucking"—conditions which are particularly undesirable in the postpartum cow or mare. Recommended treatment consists of parenteral antibiotics and local treatment of lacerations by suturing early, or application of protective mild antibiotic dressings. Tetanus antitoxin or a booster injection of toxoid should be administered in the mare.

Hematomas and Contusions of the Vagina or the Vulva are occasionally noted in all animals but most commonly in the mare and sow. They may be confused with or mistaken for tumors or prolapse of the vagina or bladder. Hematomas involving the vaginal wall are found on examination of the genital tract. In rare instances they may be observed protruding between the vulvar lips. A temporary Caslick's operation closing the dorsal portion of the vulva will prevent the protrusion, contamination and irritation of the vaginal hematoma. Hematomas of the vulva are readily noted. If left alone they are usually absorbed within 1 to 3 weeks. In some cases they may rupture through the mucous membrane or the owner of the animal may request that they be removed; this can be done by incising, removing the clot and carefully suturing to control further bleeding and to obliterate the area that contained the large blood clot. This should not be performed until after 3 to 4 days following parturition. In occasional cases diagnosed early, ice packs or cold water spray might be indicated. Contusions of the vulva, vagina, and cervix resulting in swelling and edema, occur most frequently due to trauma during fetotomy operations or from external injuries.

Occasionally in the sow hematoma of the vulva may rupture and cause serious or fatal hemorrhage. To control or prevent such hemorrhage the labial branch of the internal pudendal artery should be ligated by inserting a

heavy Vetafil or umbilical tape suture at the junction of the vulva and the semimembranosus muscle in the dorso-lateral quadrant of the vulva, at about 2 to 3 o'clock (9 to 10 o'clock) into lumen of vulva and out again through the dorsal mucosa and skin at about 12 to 1 or 11 to 12 o'clock. This ligature can be removed in 5 to 7 days. Mechanical protection of the vulva can be provided by placing a piece of plywood behind the sow at a 60 to 70 degree angle to the floor of the farrowing stall with the uppermost end nearest the sow.^{12a,27}

Occasionally a blow or a kick in the region of the clitoris will result in marked edema of the clitoris and vulva in the mare. In most cases these swellings subside fairly promptly and should not be confused with edema from the udder that may extend upward and involve the vulva in cattle. If edema is severe, alternate cold and hot applications, massage, and in certain cases small punctures or incisions through the mucous membrane may release the fluid or reduce the edematous swelling of the vulva.

Contusions of the Maternal Pelvic Structures by the fetus or by instruments used during fetotomy may result in intrapelvic hematomas and hemorrhages, or may cause obturator or gluteal paralysis by injury to those nerves at parturition. **Gluteal paralysis** is rare and is described only in the mare; it is brought about by contusions caused by a bony prominence on the fetus pressing on the gluteal nerve as it passes over the bony portion of the lumbosacral articulation or ilium. This may be a bilateral or unilateral injury and usually occurs in mares that apparently give birth without difficulty. In this condition the mare will show some difficulty in rising and may require assistance in rising if the injury is bilateral. The gait is characterized by a definite lameness and weakness of the affected limb. After a few days to a week, a marked atrophy of the gluteal muscles on the affected side is very noticeable. After a few weeks the lameness or paralysis of the limb becomes less observable but it may take 6 to 18 months for complete recovery. The prognosis is favorable. Treatment consists of good nursing and possibly nonsteroidal antiinflammatory drugs such as phenylbutazone. The mare should be in a large, well-bedded box stall with good footing. In some cases slings or assistance in rising may be necessary for several days or a week. Affected mares should not be allowed to struggle or exert themselves in rising. External applications, massage, or other treatments are of no value.

Calving Paralysis or Obturator Paralysis may occur in the mare or cow but is most common in the latter. It is much more prevalent in heifers than in cows. Injury to the obturator nerve and lumbar (L6) roots of the sciatic (ischiatric) nerves¹⁴ is observed so often in hip lock in the anterior presentation that before this type of dystocia is

relieved calving paralysis should always be suspected. An examination is done to inform the owner of the paralysis before the obstetrical operation so that later the veterinarian will not be blamed for the injury. The condition may affect one or both rear limbs. If the cow is down and laboring with a hip lock condition, the underneath leg and nerves is the one most commonly and severely affected. This contusion is usually caused by the bony tuberosities of the fetal hips, especially the greater trochanters, contusing the obturator and sciatic nerves as the nerves either pass over the bony prominence of the lumbo-sacral articulation, or as it passes down the shaft of the ilium before it enters the obturator foramen. Calving paralysis in heifers is very common in the hip lock condition that has existed for several hours. Yet when strong forced extraction has to be applied manually or with the fetal extractor to draw a large fetus through a heifer's pelvis, calving paralysis seldom occurs. Injury to the obturator and sciatic nerves causes a paralysis of the medial and caudal adductor muscles of the thigh and partial loss of tibial and peroneal nerve function. This seriously effects the total support of the pelvic limb.¹⁴ If the condition is unilateral the cow can stand on the unaffected limb and as it walks the affected limb is moved stiffly forward and is abducted so the foot is placed on the ground 8 to 24 cm. lateral from the normal position. The cow is unsteady and is likely to slip and fall. If both nerves are bilaterally contused and injured, both limbs are stiffly extended and abducted and the cow usually is unable to rise. If assisted to its feet and the hind limbs held together, the animal can stand but when it takes a step the affected limb is extended cranially and abducted and the cow falls to the ground.

If paralysis is severe and bilateral the prognosis should be guarded. If the paralysis is mild and the animal can walk, even though with difficulty, the prognosis is good. In most cases the condition improves rapidly and in 2 to 7 days the animal is able to walk quite well. Other cases may take longer for recovery, even up to 4 to 8 weeks. In rare cases the damage to the obturator and L6 roots of the sciatic nerves may be severe and permanent. The chances for recovery after 2 to 3 weeks are poor, and slaughter may be recommended. The only treatments of any value are good nursing and tying the animal's rear legs together in order to prevent excessive abduction, over 35 to 45 cm., and possible complications of a dislocated hip or fractured pelvis. The use of straps such as hame straps around the pasterns tied with a length of rope or chain aids in preventing abduction of the limbs and helps the animal to rise. Some veterinarians strap or tie the hocks together but it is difficult to fasten straps or ropes above the hocks tightly enough so that they do

not slide down, and yet loosely enough to allow movement of the gastrocnemius tendon. In the mare and occasionally in the cow the use of slings may be of value in assisting the animal to rise to its feet and supporting it for a short period. The animal should be kept in a well-bedded large box stall or pen, preferably with a dirt floor. Under such conditions dairy cattle should be milked by rolling the cow first to one side and then to the other. Possibly treatment with the anterior inflammatory non-steroidal drugs such as phenylbutazone may be helpful.

Peroneal paralysis due to injury or trauma to the peroneal nerve as it passes over the dorsolateral condyle of the tibia and fibula is observed in cattle confined in stanchions with their rear parts over the edge of the gutter. It occurs most often in cows with dystocia and hypocalcemia that struggle to rise (See Figure 94). Injury to the peroneal or fibular nerve results in anesthesia of the cranial surface of the fetlock and metatarsus and paralysis of the muscles that extend the digit and flex the hock, namely the long and lateral digital extensors, the peroneus tertius and the anterior tibial muscles. This results in knuckling of the fetlock and dropping of the hock and difficulty in rising, standing and walking.²⁵ As with injury to the obturator nerve good nursing care and close confinement are essential. A rigid supporting bandage to the lower leg may prevent knuckling of the fetlock. Peroneal paralysis should be differentiated from rupture of the gastrocnemius muscle and posterior paresis due to



Figure 94. Bilateral peroneal nerve injury and paralysis in a cow.

lesions in the spinal cord. Rarely other paralyses may be observed following dystocia or injury at the time of parturition including brachial or radial nerve paralysis in stanchioned cattle in which the forelimb was caught in the manger and forcefully extended. These miscellaneous nerve paralyses have been well-demonstrated.⁶²

Rupture of the gastrocnemius muscle is apparently secondary to Zenker's degeneration of the muscle and usually follows considerable struggling or efforts to rise during dystocia, hypocalcemia or after epidural anesthesia (See Figure 95). Zenker's degeneration may be due to excessive muscular activity especially in cows that have been confined for long periods and provided very limited exercise. Furthermore it is seen more often in states where selenium is known to be deficient.⁴² Eleven cases of rupture of the gastrocnemius muscle were reported,³⁶ in 3 high-producing Holstein herds in one year in south-central New York State where selenium is deficient. The condition may be diagnosed by the inability to support weight on the affected leg, the flaccid gastrocnemius tendon and the hard swelling due to edema, hemorrhage and Zenkers' degeneration in the gastrocnemius muscle. Mild cases that can stand may recover in several weeks if they are confined and possibly a support such as a metal brace or Thomas splint provided. In most advanced cases slaughter is indicated. Prophylactic injections of selenium or selenium provided as a trace mineral may be indicated in selenium deficient areas.

Rupture of the Uterus, Cervix, Vagina, and Perineum

Uterine or Vaginal Rupture may occur in any species.^{3,22,33,35,43,46,48,55} It may be due to prolonged dystocia

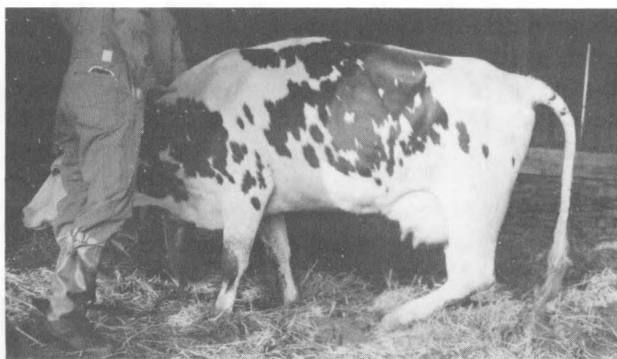


Figure 95. Unilateral rupture of the gastrocnemius muscle in a cow during postparturient paresis.

with fetal emphysema; torsion of the uterus, in which transverse rupture may occur in prolonged cases; to improper manipulations and traction on the fetus; to fatigue of the operators, or to an accident in fetotomy operations in large animals or to forceps removal of a fetus in bitches; to protruding bones of the fetus after fetotomy; or due to inexperienced manipulations of the fetus by laymen. The author has observed a ewe with maternal intestines in the vagina due to a ruptured uterus caused by an owner with large hands attempting to relieve a dystocia. For this latter reason and others associated with prolonged dystocia, the uterus and vagina should be carefully examined prior to any obstetrical operation to be certain that a rupture of the uterus, cervix, or vagina is not present. Rupture produced by the operating veterinarian even if due to his fatigue is extremely embarrassing and should be avoided. In 26 cases of uterine rupture in cows out of 1004 referred obstetric cases to a college clinic, 7 cows had uterine torsion, 7 had oversized fetuses, 4 had emphysematous fetuses, 3 had fetal monsters and 2 had an immature pelvis. Nineteen of the 26 cows recovered after surgery.³⁵ In the birth of fetuses with long extremities, such as the foal, vaginal rupture may be due to improper presentations, positions, and postures, especially dorso-pubic positions, anterior longitudinal presentations with the hind limbs extended beneath the body, transverse ventral presentations, and when the forefoot or feet are crossed over the neck. This latter presentation may result in rupture of the vagina, rectum and perineum (See Figure 96). Rupture of the uterus is common in the mare in rotated bicornual pregnancy if traction is applied to the fetus. Forced extraction of a bovine fetus in a normal presentation may cause rupture of the uterus, cervix, or vagina by forcing these structures against a sharp bony prominence occasionally found on the cranial portion of the pubic symphysis. Transverse rupture of the uterus may be caused by retraction or contraction rings of the uterine wall; or rupture of the cervix if the cervix is poorly dilated; rupture of the vagina may occur if perivaginal fat is pushed caudally as the fetus is forcibly drawn toward the vulva. In this latter instance the vaginal wall near the hymenal ring or vestibular-vaginal border ruptures to allow the escape of the fat. A similar tear or rupture of the vagina occasionally results in a prolapse of the bladder. Forced extraction with the fetus in abnormal posture or position or in torsion of the uterus may cause a portion of the uterine or vaginal wall to be caught by a deviated extremity and folded upon itself to produce a rupture. A dry, emphysematous fetus and a swollen, dry birth canal are conducive to rupture of the vaginal, cervical, or uterine walls when strong traction or repulsion is applied. In one cow rupture of the uterus occurred

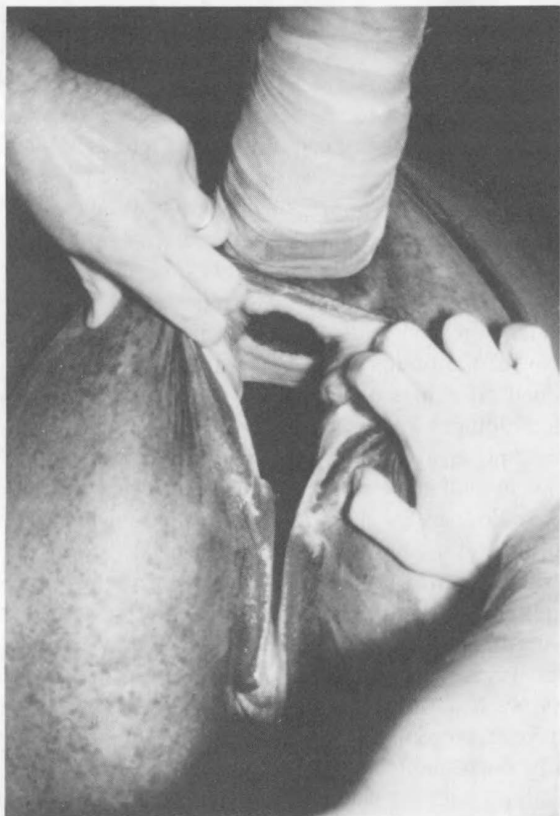


Figure 96. Rupture of the rectum, vagina and perineum of a mare caused by dystocia. This picture was taken 8 weeks after the accident.

apparently due to extensive severe adhesions of the uterus to the adjacent viscera. Administration of oxytocin to dogs or other animals with dystocia and/or uterine torsion may cause uterine rupture.²⁶ (See Figure 97.) In a few cases spontaneous uterine rupture may occur due to unknown causes. After each dystocia case the veterinarian should carefully examine the uterus and birth canal for the presence of a rupture of the uterus or birth canal in order that it may be treated promptly or in hopeless cases the cow may be slaughtered and some value thereby salvaged.

The symptoms and prognosis of rupture of the genital tract vary with the animal and the portion of the genital tract involved; the size of the rupture; the character of the rupture, whether regular or irregular, horizontal or vertical; the nature of the uterine contents; the amount of uterine contents that have escaped into the abdominal cavity; and whether or not intestines or bladder have prolapsed through the rent in the wall of the genital tract. In a mare unless the uterine rupture is small and no infection was present in the uterus, a fatal peritonitis usually develops rapidly. In the cow or other domestic an-

imal rupture of the uterus due to an emphysematous fetus rapidly produces a fatal peritonitis. A similar termination can be expected in a uterine rupture in any animal in which the uterine contents are severely infected. In rare cases in cows, a rupture of the uterus may occur which releases a live or recently dead fetus into the abdominal cavity. Occasionally the symptoms of uterine rupture in the cow may be slight, but usually anorexia, lack of ruminations and rumen contractions, restlessness, rapid pulse and respiration rates, and cold extremities are present. The body temperature is usually normal or subnormal but may occasionally be elevated. If infected fetuses and material are released into the abdominal cavity, acute, severe septicemia or shock symptoms develop rapidly. Prostration, and death usually occur in 1 to 2 days. In less severe cases peritonitis is less marked and the animal may survive with the fetus becoming walled off, or death may occur in 3 to 7 days. The fetus may be removed through a laparotomy incision and the uterus sutured. With proper technique and aftercare some of these cases will survive. In small ruptures of the uterus after parturition or dystocia when no infection is present and the rent is in the dorsal half of the uterus some cows have survived after repeated doses of oxytocin and with parenteral antibiotic therapy. In these cases penicillin (three to six million units), and streptomycin (4 to 5 gms.), or **Aureomycin** or **Terramycin** or tetracycline in 2- to 4- gm. doses or similar antibiotic therapy is given daily to the average 800- to 1000-lb. cow or mare. One to two grams of the latter broad-range antibiotics should be placed in the uterus to control intrauterine infection. The administration of antibiotics and of sodium sulfonamides in concentrations of 5 to 10 percent, through the abdom-



Figure 97. Transverse rupture at parturition of the isolated uterine horn containing canine fetuses—this condition apparently followed trauma or torsion of the horn at about midgestation resulting in the separation of the horn from the rest of the uterus, note the scarring.

inal wall into the peritoneal cavity might be indicated in some cases. Occasionally the uterine rupture is large enough to require suturing. This is difficult in cows, but may be performed by working through the birth canal, using continuous or mattress sutures to bring the serous surfaces of the uterus on either side of the rupture into apposition. Some veterinarians have recommended prolapsing the uterus or vagina by pulling it to the outside through the birth canal and then suturing the rent and replacing the organs. A few veterinarians have successfully prolapsed the severely lacerated uterus through the birth canal and amputated it.¹³ In large animals suturing the uterus through a laparotomy incision may be successful or it may be sutured in this manner with assistance through the birth canal. The presence of a retained placenta, septic metritis, an atonic uterine wall, or prolapsed intestines results in a poor prognosis. In most severe cases of uterine rupture in the cow, ewe, or sow the prognosis is poor and slaughter is usually advised if the animal is in an otherwise satisfactory condition. Even if recovery takes place, the future breeding life of that animal is very questionable, as chronic perimetritis and peritonitis are the probable results. In the bitch uterine rupture, as in the larger animals, is usually characterized by anorexia, depression, weakness; in the early stages an elevated and in late stages a depressed body temperature; rapid pulse and respirations; cold extremities; constipation, or fetid diarrhea; pale mucous membranes especially if there is internal hemorrhage or shock; followed by prostration and death in 1 to 3 days. In the bitch laparotomy and hysterectomy, if performed early, together with flushing of the abdominal cavity with warm saline solution and antibiotics, and treatment to prevent shock and infection, occasionally results in recovery of the bitch. In all species except the mare extrauterine fetuses may be walled off or encapsulated as described previously. Under no circumstances should fluids be injected into the ruptured uteri nor should manipulations of retained placentas take place. The latter should be allowed to drop from the uterus without assistance. Complete rupture of the cervix in large animals is similar to rupture of the uterus but because proper suturing of this structure is so difficult, the prognosis is poor if the rupture is extensive.

Rupture of the vagina is usually not as serious as uterine rupture and the prognosis is much better unless the rupture extends into the peritoneal cavity. Simple ruptures of the vagina especially of the lateral or dorsal wall need not be sutured unless the operator desires to do so. In most cases there is no need to suture small ruptures even on the floor of the vagina, but some veterinarians prefer to do so in order to prevent a possible perivaginal abscess if a retained placenta or metritis occurs. In rare cases these perivaginal abscesses, which may also occur

secondary to an infected perivaginal hematoma, become large and finally after 2 to 6 weeks or more break out between the vulvar lips and the tuber ischii. Mild wounds of the vagina heal rapidly. Recto-vaginal fistulas due to rupture of the dorsal wall of the vagina and ventral wall of the rectum are occasionally observed, especially in mares in which parturition is violent. If these are noted promptly they should be sutured immediately, care being taken that the rectal wall is tightly sutured in a transverse manner. Suturing of the vaginal wall is not as essential. If 24 to 48 hours pass before this condition is noticed it usually is impossible to correct at that time and one must wait until the edema, swelling, granulation tissue, and wound edges have completely healed before surgical intervention is undertaken to correct the fistula.^{57b} In these chronic cases some feces and a mucopurulent discharge are expelled from the vulva. If the fistula is small, the rectum may be packed with cotton and the vagina douched with saline before breeding. If pregnancy occurs the fistula may then be sutured without the loss of a breeding season.

Due to straining, rupture of the uterus may be followed by prolapse of the intestines into the uterus or birth canal or through the vulva. If rupture of the vagina or cervix extends into the peritoneal cavity it may also result in prolapse of the intestines. The bladder or fat may prolapse through a rupture in the ventral or lateral wall of the vagina. These conditions will be discussed later.

Rupture of the Perineum and Vulva is observed chiefly in the mare but may occasionally be observed in cows and possibly ewes when excessive traction is applied to rapidly remove the fetus. Thus the vulva and perineal region may be ruptured before it has time to dilate gradually. This condition has been rarely observed in dairy heifers; hemorrhage may be severe and in some cases fatal.^{59,60} More often it is observed in the mare in which the forelegs and even the nose in anterior presentation or in the dorsopubic position the long limbs of the equine fetus may be pushed dorsally into the vaginal roof and rectal floor. This sacculated portion, due to the violence of parturition, is forced into the dilated anus. (See Figure 96.) The vagina and rectal floor rupture, the feet protrude from the anus, and as the fetus is expelled the vulva and anus are torn longitudinally. In rare cases the vulva and vestibule remain intact and the fetus is expelled through the ruptured rectum, anus and perineal tissues. The presence of the ruptured perineum or "gill flirter" condition causing the rectum and vestibule to become a continuous cavity or "cloaca" is readily noted. As in recto-vaginal fistula it is advisable to correct and suture the rupture immediately, paying particular attention to suturing the rectal wall and anal sphincter. If the operation is not performed at once it must be postponed

about 6 weeks until the swelling and granulation tissue has subsided and the wound has completely healed.^{57b} If these mares are not operated upon the feces drop into the vagina, the vulva and vaginal mucous membranes are irritated, and the animal sucks air, pneumovagina, and there is a profuse discharge of mucus and feces that soil the rear parts. This condition is seldom observed in the cow but mild vulvo-anal lacerations and ruptures are seen especially in beef heifers and rarely in ewes. Proper use of episiotomy operations in cattle would prevent this condition. The prognosis for the life of the patient is good if hemorrhage or shock is not immediately fatal. If the condition is not corrected, the future breeding life of the animal is poor. Very rarely "gill-flirter" mares may conceive. The prognosis for this operation is usually guarded. For a discussion of this operation and that of the recto-vaginal fistula the author recommends the standard veterinary surgical texts the detailed anatomy of the perineal region of the mare,²³ and a description of the operation in the mare and cow.^{1,5,8,50,57b} The author particularly commends the technique of a two-phase operation for the surgical repair of third degree perineal lacerations and rectal vaginal fistulas.¹ The first operation produces a firm shelf of tissue between the rectum and vagina by suturing the scarified tissues between the rectum and vagina and the vaginal mucous membrane but not placing sutures through the rectal mucosa. In about 2 weeks the second operation is performed that closes and reforms the perineal area, the anus and vulva.

Rupture of the pelvic and abdominal organs other than the genital tract during birth or dystocia have been described rarely in the cow and mare. A rupture of the rectum in cows has been described.^{16,56} Four cases were reported²⁰ where the free end of the cecum ruptured through the rectal wall. In all these cases the fetus was in posterior presentation. Rupture of the intestine of cows has been described.^{47,48} Rupture of the cecum and ventral colon have been reported during parturition in the mare.^{17,28,57a} Death always occurred in mares after rupture of the intestine and usually occurred in cattle. A few cows operated on immediately after the rupture survived. Rupture of the bladder may occur occasionally in the mare and cow.^{7,45,58b} In very rare instances rupture of the diaphragm in a mare may result from violent straining.

Prolapse of the Abdominal or Pelvic Viscera

Prolapse of the Intestines may occur through a rupture or laceration in the uterus, cervix, or cranial portion of the vagina at the time of parturition. The intestines

may only enter the uterus or may pass into the vagina and out the vulva. This condition should be differentiated from a **Schistosomus reflexus** or a ruptured umbilical hernia of the fetus. The prognosis is invariably poor, since the dystocia causing the rupture usually is severe, contamination and infection of the intestines and abdominal cavity is probable, and it is difficult to control the intestines to prevent their injury during removal of the fetus. Slaughter of the animal is usually recommended. In occasional cases in which infection or trauma to the intestines is minimal, replacing the intestines, suturing the rupture and removing the fetus might be possible. Closure of the rupture wound in the uterus may be accomplished through the birth canal, or probably a better approach would be through the laparotomy incision after a cesarean operation. If the intestine is traumatized or severely contaminated resection of a portion of it may be necessary. Perforating lacerations or ruptures of the cervix and anterior vagina are sutured through the birth canal.^{21,58} Aftercare consists of carefully suturing the rupture, and administering local and parenteral antibiotic treatment to control peritonitis, as recommended for the handling of uterine rupture. **Left displacement of the abomasum** is a fairly common occurrence after parturition in the cow.

Prolapse of the rectum may occasionally occur in any animal in dystocia or other causes associated with persistent violent straining and a relaxed anal sphincter. Slight eversion of the rectum at parturition is common, but severe prolapse is rare. In the mare prolapse of 2 to 3 feet of rectum is usually fatal since rupture of the rectum or small colon often occurs secondarily. If prolapse of the rectum begins in the mare it should be controlled by holding the rectum in place forcibly with a towel over the anus until the fetus is expelled or withdrawn. In other species prolapse is neither as serious nor as extensive. It should be prevented if possible or replaced promptly before or after the fetus is removed. A purse-string suture of heavy nylon material around the anus is often indicated after replacement. If unnoticed until trauma and edema are present, surgery, including either the sub-mucosal resection reefing operation or amputation, together with retaining sutures may be necessary to replace and maintain it in position. The different types of equine rectal prolapses and their correction was reviewed.⁵²

Prolapse of the Bladder may occur in all species but it is seen most commonly in the larger domestic animals before or after parturition. Prolapse of the bladder usually takes place through a rupture or tear in the floor of the vagina and the bladder is noticed hanging from the vulvar orifice after parturition. Due to the sharp bend in the urethra the prolapsed organ fills with urine. This con-

dition must be differentiated from eversion of the bladder through the urethra, vaginal or vulvar tumors, cysts, a mass of fat protruding through a rupture in the floor of the vagina, or vaginal or vulvar hematomas.⁵¹ If the bladder is distended with urine it may be replaced and the urine forced out or it may be drained with a needle before replacing. The external surface of the bladder should be carefully cleaned, covered with an antibiotic solution, and the organ replaced. The rupture in the vaginal floor permitting the prolapse should be sutured and the animal placed on parenteral antibiotics.

Eversion of the Bladder has been described mainly in the mare, in which the urethra is large and parturition violent. It has only very rarely been seen in the other animals such as the cow or sow.^{17b} In rare and serious cases in the mare intestines may prolapse into the everted bladder and prevent reduction.^{24,55} Eversion of the bladder may occur before or during parturition. It seldom if ever obstructs the passage of the fetus but occasionally the everted bladder and urethra may be severely traumatized when the fetus passes through the vestibule. Eversion of the bladder is easily recognized, as this organ is attached to the area of the ventral floor of the vulva where the urethra orifice is normally located. The everted bladder is pear-shaped. The openings of the two ureters drip urine and the mucous lining of the bladder may be noted and felt. If the everted bladder is small it may not become exposed through the vulvar lips until the animal lies down. In handling eversion of the bladder, the bladder should be thoroughly cleansed. If a tear or rupture is present it should be sutured or if a portion is damaged severely that portion might be removed and the edges of the incision sutured. Following the injection of epidural anesthesia, the operator should use both hands to compress the bladder and force it back through the urethra. The bladder should be massaged and pressed through the vagina floor until it is in its proper position. Aftercare consists of irrigating the bladder with saline solution and antibiotics and administering antibiotics parenterally so that the urine will contain a high concentration of the antibiotic for a number of days. It is seldom necessary to place a stitch in the external urinary meatus to prevent another eversion once the fetus has been removed and labor has ceased.

Prolapse of Perivaginal Fat may occur through a small rupture of the caudal portion of the vagina during forced extraction of the fetus especially in fat dairy or beef heifers. These masses of fat should be differentiated from prolapse or eversion of the bladder, as they are likely to resemble those structures. On examination, the vaginal rupture, which is usually quite small, may be found at the base of the prolapsed mass of fat. This fat may be

cut off with a knife or scissors, as there will be little bleeding. The vaginal rupture may be sutured or left to heal without suturing. Sulfonamide powder or antibiotics are customarily placed in the wound before suturing. The prognosis is good as a perivaginal abscess seldom develops.

Prolapse or Eversion of the Uterus may be called casting of the "wethers" or casting of the "calf bed." It is observed most commonly in the cow and ewe, occasionally in sows,^{12a} and rarely in the bitch, queen and mare. It occurs most often immediately after parturition and occasionally up to several hours afterward. In rare cases it may occur 48 to 72 hours after parturition. In bitches there may be rare cases of prolapse of one horn while fetuses are still in the other horn.¹⁰ Prolapse of the uterus is predisposed by long mesometrial attachments; violent or strong tenesmus; a relaxed, atonic, flaccid uterus; retention of the placenta especially at the ovarian pole of the gravid horn in cows and of the nongravid horn in mares; and by excessive relaxation of the pelvic and perineal region. In dairy cows it is commonly seen in confined or stabled cattle during the winter months that calve in a stallion with their rear parts sloping downwards and hanging over the gutter. The use of great force in forced extraction of the fetus predisposes to tenesmus after relief of the dystocia. If the uterus is not contracting it frequently prolapses immediately after relief of the dystocia. Prolapse of the relatively flaccid uterus in older cows is frequently associated with hypocalcemia at parturition.^{5,32} Dystocia associated with a mild hypocalcemia was present in 42 percent of 26 beef cows with uterine prolapse compared with only 6.7 percent of the control animals.³⁸ In dystocia when the uterus is contracted tightly around a dry fetus, forced extraction is likely to result in prolapse of the uterus. Prolapse of the uterus is seen most commonly in pluriparous dairy cows but is not infrequent in poorly grown, thin, debilitated dairy heifers. Prolapse of the uterus was frequently observed in sheep in Australia due to a hyperestrogenism from eating clovers high in estrogenic hormones. Prolapse of the uterus is apparently not hereditary although occasionally it may be seen in dam and daughter. There was a probable hereditary basis for prolapse of the uterus and vagina in Hereford cattle.⁶¹ A low plane of nutrition may also be a factor. Prolapse of the uterus very rarely occurs following prolapse of the vagina prior to parturition despite the common belief among owners that if the cow prolapses the vagina prepartum it is apt to suffer prolapse of the uterus postpartum. Prolapse of the uterus rarely recurs at a subsequent parturition.

In a Norwegian study³² of 955 cows treated by 171 veterinarians for prolapsed uterus, 27 percent occurred

within 1 hour, 48 percent within 3 hours, 65 percent within 6 hours and 90 percent within 15 hours after calving. Numerically uterine prolapse was most common in primipara but the highest incidences, 3 times higher than first and second calvings, occurred in cows at their fifth or greater calving where it was related to hypocalcemia. Of 506 cows that prolapsed, only 18 had prolapsed at 1736 prior calvings, an incidence of about 1 percent. About 1 percent of cows with vaginal prolapse prior to calving developed uterine prolapse after calving. At the time of uterine prolapse 56.6 percent of the fetal membranes were still attached. Of 955 cases 83 percent recovered. Of those not surviving 35 percent died before or during treatment, 24 percent were slaughtered because of uterine injury or irreplaceable prolapse, 16 percent died shortly after treatment and 24 percent died or were slaughtered later in the course of the illness. Deaths were highest in cows with both a prolapsed uterus and hypocalcemia. Of 407 cows with prolapse that were rebred 78.4 percent conceived. Breeding after 90 days postpartum resulted in normal conception rates. In only 6 cows did the prolapse reoccur within a few days. Thus suturing the vulva to prevent subsequent prolapse is not necessary.³²

The symptoms of prolapse of the uterus are obvious. (See Figure 98.) The animal is usually recumbent but may be standing, with the uterus hanging to the hocks. Retention of the placenta is likely. The fetal membranes and/or mucous membrane of the uterus is exposed and usually covered with feces, straw, dirt, or blood clots unless of very recent occurrence. The uterus is usually enlarged and edematous especially if the condition has existed for 4 to 6 hours or longer. Excellent illustrations of the condition in various species of animals have been made.¹⁰ In the cow the gravid horn prolapses or everts sufficiently so that the cervix is usually present at the vulva. The nongravid horn is inside the peritoneal surfaces of the prolapsed gravid horn and does not evert because of the strong intercornual ligament. The opening of the nongravid horn may be observed as an oval or slit-like orifice near the vulva on the ventral or lateral side of the prolapsed gravid horn. Prolapse of the uterus in the ewe is similar to this condition in the cow. In the other species, horses and multipara, usually one horn—or rarely both horns—may be prolapsed or everted. Ninety percent of the uterine prolapses in sows were bicornual with the initial invagination occurring in the uterine body.⁵⁴ In cows the initial invagination also occurred at this site. Prolapse or invagination also occurred at this site. Prolapse or invagination of the uterine horn should be differentiated from a prolapse of the vagina. In the bitch and queen palpation of the abdomen may reveal the



Figure 98. Uterine prolapse in a Hereford cow.

thickened invaginated uterine horn and abdominal pain. In the mare the uterine body may compose the major portion of the exposed everted uterus. In most animals prolapse of the uterus results in mild to moderate symptoms of tenesmus, restlessness, pain, anxiety, anorexia, and an increase in pulse and respiration rate. In cases with complicating factors of internal hemorrhage due to rupture of one of the uterine vessels, shock, incarceration and ischemia of intestines present in the peritoneal sac of the prolapsed uterus due to pressure obstructing the circulation of the intestines, or other diseases such as hypocalcemia may cause the animal to be recumbent. A very rapid, weak pulse, irregular, rapid respiration rates, pale mucous membranes, expiratory grunt, and prostration with severe depression and inability to rise indicate serious complications. When intestines or excessive hemorrhage with a large blood clot are present in the peritoneal sac formed by the prolapsed uterus, the bovine uterus may be 30 to 45 cm. or more in diameter. In ewes, intestines frequently are present in the prolapsed uterine horn.

The prognosis in uterine prolapse varies greatly. In

most cases in which the condition is observed early, the veterinarian called promptly, the cow able to stand and the uterus not severely injured, the prognosis for the life of the cow is good. In 158 cases of prolapse of the uterus in dairy cattle seen from 1943 to 1953 in the Ambulatory Clinic of New York State Veterinary College, the mortality rate was 18 percent. If cases obviously complicated by other conditions were eliminated the mortality rate in cows in good physical condition at the time of the operation would probably be 5 percent or lower. The prognosis is poorer in beef cattle on pasture, where the condition may not be observed as early and aid secured promptly.⁶¹ The animals' future breeding history may be good or poor depending upon the severity of the uterine lesions, the promptness of treatment and the rate of involution. If the uterus is grossly contaminated, or dried due to exposure to the sun, or if lacerations are present, the prognosis is more guarded due to the possibility of a septic metritis, perimetritis or peritonitis developing, and the prognosis for the future breeding life of the animal is questionable. It is surprising how much trauma, irritation, and contamination the uterus can withstand. Upon replacement of the organ this infection is overcome, the traumatic lesions heal, and the animal recovers. In other cases, with the animal prostrate, unable to rise and conditions complicated by shock, internal hemorrhage, or incarceration of the intestines, the prognosis is usually very poor to hopeless. In the author's experience, mainly with dairy cattle, the percentage of cases of uterine prolapse that terminated fatally due to internal hemorrhage, shock, or incarceration of the intestines was high when the cows were in stanchions and the prolapsed uterus had dropped into the gutter. This is further reason for having box stalls for calving cows or having them calve on pasture. If other diseases are present, such as hypocalcemia or obturator paralysis, the prognosis is based on the severity of those conditions as well. In cattle in which the uterus is so badly damaged or diseased that replacement cannot be considered and amputation of the uterus is the only recourse, the prognosis is poor although some of these cases may survive.

In the ewe the prognosis for prolapse or eversion of the uterus is similar to that of the cow. In the mare the condition is more serious, but if the animals are treated promptly most will survive. Amputation of the uterus in the mare should seldom if ever be attempted since it is indicated only when the uterus is severely traumatized and lacerated, and then the prognosis is extremely grave. In the sow the prognosis is poor as extensive prolapse usually results in internal hemorrhages and shock. The author has observed 5 or 6 cases of prolapse of the uterus in the sow and all were either dead on his arrival at the

farm or died with 15 to 30 minutes. A few cases of prolapse of the uterus in sows have recovered following a laparotomy or replacement.^{5,37} In the bitch and queen the prognosis is fair to good even though the condition is rather difficult to handle because of the length of the uterine horns and the inability of the operator to aid replacement with his hand and arm as in the larger domestic animals. Laparotomy and replacement of the uterus in the abdomen may be necessary in the bitch, queen and sow. Ovario-hysterectomy is more frequently and successfully performed in the bitch and queen than in the larger animals.¹⁸ Following proper replacement of the prolapsed uterus very few cases recur in any species.

The treatment or handling of prolapse of the uterus in the cow can be made much easier if the owner is instructed to wrap the cow's uterus in a wet towel or sheet or to place it in a plastic bag to keep it moist and clean until replaced. If the cow is standing the uterus should be raised and supported level with the vulva until assistance arrives. If the cow is recumbent in a stanchion the gutter should be built up to support the uterus and keep it from hanging. This prevents the uterus from becoming edematous and may possibly prevent rupture of the uterine vessels. If possible the cow should be in or near the barn, in a clean paddock or well-bedded stall to make the operation cleaner, more convenient, and less difficult. Good light is essential. Proper restraint of the animal aids in prompt and easy replacement of the everted uterus. Epidural anesthesia should be used routinely in sufficient dosage to provide good anesthesia but at the same time to keep the animal standing. In fact some cows and mares that are down and refuse to stand may get up promptly after epidural anesthesia is given. Epidural anesthesia controls and prevents defecation during replacement of the uterus. Elevation of the rear parts greatly facilitates replacement of the uterus. The ordinary standing posture of the cow usually gives sufficient elevation of the rear parts. If replacement is to be made even easier the fore feet may be lowered or the rear parts elevated by making the animal stand on a slope. If the animal is recumbent and refuses to rise and cannot be stimulated to do so by prodding with a sharp object or an electric prod, by rolling her tail beneath the foot, or the intravenous injection of calcium gluconate, benzydrene stimulants, or 20 to 40 ml or more of Pyribenzamine, even after giving epidural anesthesia, and since it is very difficult or harmful to elevate the rear quarters of a cow that is unable to stand either manually or mechanically, a practical effective procedure is to place ropes on the rear pasterns and draw both legs out behind the cow. This tips the pelvis ventrally and greatly facilitates replacement of the uterus. Epidural anesthesia is not nec-

essary in ewes because with the aid of one or two men grasping each hind leg the rear parts can be elevated high enough so that the uterus almost falls into place. In multiparous animals, and possibly the mare, general anesthesia may be indicated.

The uterus of the cow should be carefully prepared for replacement. It should be held level with the ischial arch or vulva during these operations. The purpose of this is to relieve pressure on the broad ligament and uterine veins as they pass over the ischial arch, and to restore normal circulation in the prolapsed uterus. This avoids further edema of the uterine wall and aids in absorption and disappearance of the edema already present. This position of the uterus permits the bladder to resume its normal position and if intestines are present in the uterus they return to the abdominal cavity. The danger of possible rupture of the vessels in the broad ligament is greatly reduced and the cow is more comfortable when the uterus is held level with the vulva. This can be done by supporting the uterus in a towel or sheet held by a man on either side of the rear quarters of the cow, or it may be supported on a wooden or metal tray, or held in the arms of the veterinarian if he is suitably attired in a rubber apron, gown, or coveralls. The afterbirth, if present, should be gently removed. Only rarely is the afterbirth attached so securely it cannot be removed. If the removal of the placenta is impossible without severe trauma and hemorrhage resulting, it may be left in place. Following replacement of the uterus, the placenta is handled in the same manner as retained placenta in a cow not affected with prolapse of the uterus.

The uterus should be cleansed thoroughly with a warm physiological saline solution, or with water to which a small amount of mild antiseptic such as chlorine or quaternary ammonium compound has been added. To cleanse the uterus thoroughly may require 5 to 10 gallons of water. Usually if the farmer is warned at the time of the call to have plenty of hot water available, it will be ready, but if it is not available, the veterinarian should be equipped to take some with him. In some cases it may be necessary to use cotton to help clean and wipe the uterus. The adjacent vulva and perineal region should be carefully washed and cleansed at the same time, particular attention being given to folds and creases in the skin. If the uterus is lacerated, torn, or perforated, it should be carefully sutured bringing the serosal surfaces in apposition. If hemorrhage from the surface of the uterus is severe the vessel should be ligated. If prolapse of the uterus has been present for some time and edema is severe, the massage of washing the uterus and the holding of the uterus level with the vulva may not be sufficient to readily reduce its size so that it can be replaced. Vig-

orous massage of the uterus with the palm of the hand, with the fingers extended but held tightly together, may be accomplished by wrapping a towel or piece of sheeting tightly around the uterus and applying pressure through the towel without the danger or possibility of forcing a finger through the uterine wall or edematous mucosa. The author believes that the practice of applying sugar to the edematous uterus on the theory that it removes fluid through the endometrium is crude, unscientific, and not necessary. Probably most of the edematous fluid removed when sugar is massaged into the swollen uterus is forced out through small fissures produced in the endometrium by the sharp granules. It may be well to palpate the bladder before replacing the uterus, since in rare instances it may be distended and require catheterizing so that it will not interfere with the operation.

Some veterinarians advise giving 30 to 50 units of oxytocin or pituitrin to contract the bovine uterus when it is ready for replacement. The author does not advise this, inasmuch as it makes the uterine wall tense, contracted, and difficult to return to its normal position without a portion of the horn remaining invaginated. On several occasions when the prolapse occurred 36 to 72 hours after parturition and oxytocin was administered before replacement, the contracted, tense uterus could not be replaced through the contracted cervix until the uterine walls had relaxed. Many veterinarians advise coating the prolapsed uterus with oil or ointment containing a mild antiseptic or antibiotic. In replacing the uterus it should be held above the level of the floor of the pelvis; the vulvar lips should be pulled apart, and first the ventral portion and then the dorsum of the prolapsed portion of the uterus should be replaced, starting at the cervical end of the uterus nearest the vulva. Since the uterus is still more or less in the form of an arc, replacing 3 or 4 inches of the ventral or concave portion of the prolapsed horn is accompanied by replacement of 6 to 8 inches of the dorsal or convex portion of the horn. In replacing the uterus, pressure should be exerted with the palm of the hand, with the fingers extended but held tightly together, to avoid perforating the uterus. Finally the ovarian pole of the uterus is pushed by the fist through the vulva, vagina, and cervix, into the uterine cavity. If the cervical rings are contracted, pulling them gently backward with one hand and working the uterus through with the other is helpful. The ovarian pole is pushed through the vagina, cervix, and uterus with the clenched fist and arm by a piston-like or shaking motion on various parts of its perimeter until the horn is completely straightened out and no invagination is present. This is of great importance to prevent possible necrosis of the invaginated pole of the uterine horn. One should use care

not to tear or remove a caruncle and thus cause bleeding. If the uterus has been sutured no douching should follow replacement. If complete replacement of the ovarian pole is difficult the introduction of 2 to 3 gallons of very warm water or physiological saline solution into the uterine cavity is often of assistance, since it stimulates uterine contractions and helps to wash out uterine debris. This fluid should be siphoned out. Most cases do not require douching.

After the uterus is replaced properly and completely, 30 to 50 units of oxytocin should be given intramuscularly or intravenously. If it is given by the latter method the uterine wall will contract tightly on the operator's arm within 30 to 60 seconds. Following replacement, most veterinarians use a uterine antiseptic or antibiotic such as those described in treating retained placenta. Probably one to two gms. of a tetracycline or similar antibiotic is most efficient in controlling infection. In treating valuable cows another dose of oxytocin might be administered in 2 to 4 hours. If the cow is standing and not straining, a recurrence of the prolapse is very rare. Temporary suturing of the vulva with a figure of eight or mattress suture of umbilical tape into the hair line, or some other type of vulvar suture described under vaginal prolapse, or the application of a truss for 1 to 3 days is a placebo for the farmer. Very rarely does a prolapse recur if the uterus is properly replaced in a cow. If the owner has the cow under close observation for the next 3 days, as he should, a rare recurrence of the prolapse can be treated promptly. This is much better than having, as the author did in one cow, the prolapse recur into the vagina, and because of the vulvar sutures it went unnoticed for 3 days. It was impossible to replace at that time and the cow was slaughtered. A cow that failed to conceive following a prolapse of the uterus was examined and on finding no evidence of the uterus on rectal examination, a small involuted uterus was present in the vagina protruding through the cervix.¹⁹ If vulvar sutures are used they should be removed in 24 hours. Pessaries are not recommended, as they tend to cause straining. If the cow continues straining following replacement of the uterus it may be due to invagination of the ovarian pole of the uterine horn or an irritation or inflammation of the vulva. The former should be corrected, and oily protectants or anesthetic ointments may be used for the latter condition, together with a long-lasting epidural anesthetic. If the cow is recumbent the rear parts should be kept slightly higher than the fore parts for several days. If the cow can stand this is not necessary. In uncomplicated cases it is generally found that within 24 hours the cervix is closed tightly enough so that recurrence is unlikely.⁵ Parenteral antibiotics are often indicated to help

control uterine infection after replacement. In rare cases a severe or even fatal infection with metritis or peritonitis may follow prolapse of the uterus.

In the ewe the same general replacement technique is applied as in the cow but it is less difficult, since the rear quarters can be easily elevated. Recurrence is possible but vulvar sutures are also of questionable value. In these cases epidural anesthesia is valuable. Close confinement of the ewe with her rear parts elevated may be indicated. In the mare replacement is similar to the cow except that general anesthesia may occasionally be necessary. In the mare the body of the uterus is the only visible portion of the prolapsed organ.^{5,12} Tetanus antitoxin, oxytocin, antibiotics, and other supportive treatments are indicated to prevent secondary tetanus, metritis, and laminitis in the mare. In multiparous animals replacement of the uterus in the manner described in the cow is difficult, but may occasionally be possible if the rear parts of the animal are well-elevated. A laparotomy is usually necessary to accomplish the return of the uterus to its normal position. Some authors advise suturing the apex of the uterine horns to the body wall to prevent a recurrence. Occasionally in the sow and bitch one horn of the uterus prolapses and a few fetuses may still be in the other horn. Therefore in most cases in multipara a laparotomy is probably advisable. If the uterus is badly traumatized, amputation of the horn or hysterectomy is indicated in the bitch and queen and possibly rarely in the larger animals.

Hysterectomy or amputation of the prolapsed uterus is undertaken only when replacement is impossible or when it is quite certain that replacement of a badly torn, lacerated, necrotic, infected uterus possibly would result in death. In some cases where the cow is unable to rise, chickens or hogs severely mutilate a prolapsed uterus. The prognosis is always guarded to poor because of the severity of the operation and the conditions preceding it. It is contraindicated in the mare, but is often the method of choice in the bitch and queen. Although the prognosis is poor there are many recorded cases of successful amputations or hysterectomies. In the cow and ewe amputation of the uterus may be accomplished by making a long longitudinal incision in the prolapsed uterus and cervix on the dorsal and caudal surface between the rows of caruncles starting at the vulvar lips (See Figures 99 and 100). Through this extensive incision the uterine arteries and veins can be seen in the tense mesometrium. These vessels are carefully ligated in 2 or 3 places and the broad ligament is severed from the uterus between the ligatures. The cranial portion of the vagina anterior to the prolapsed cervix is easily drawn out of the vulva and is carefully ligated with fixation ligatures. The uterus

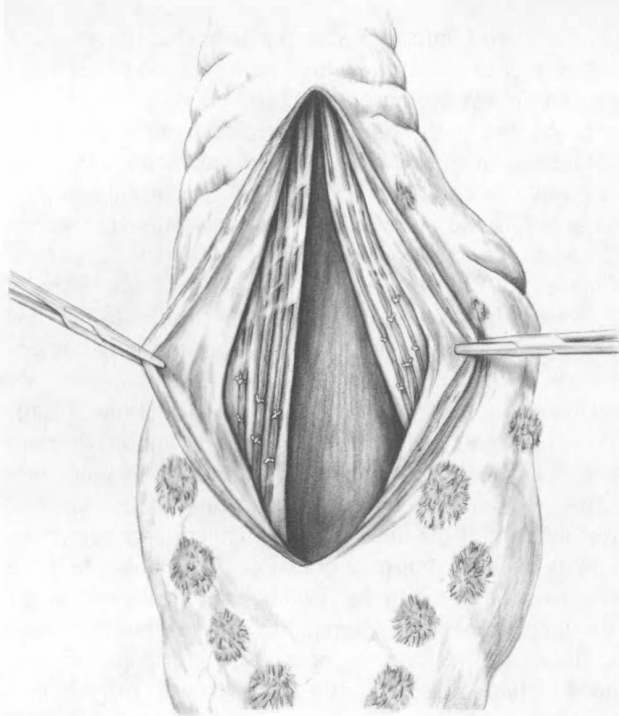


Figure 99.

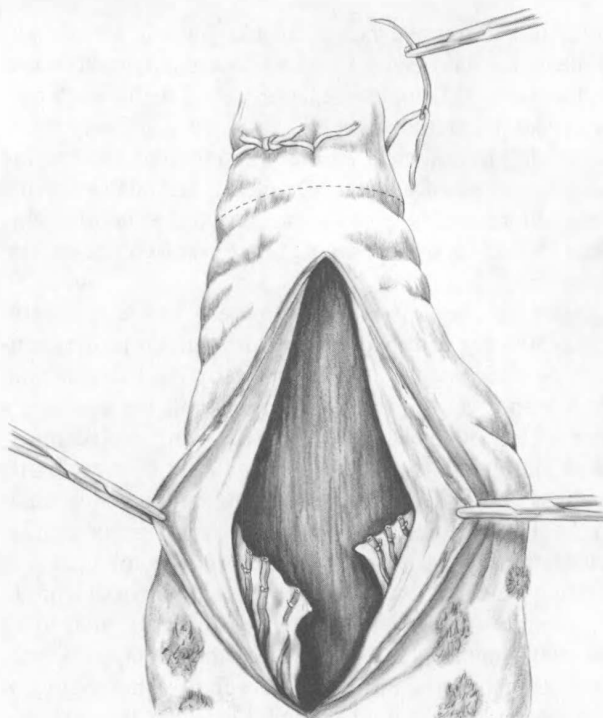


Figure 100.

A surgical technique for amputation of a prolapsed uterus in a cow. (Courtesy Cornell Veterinarian.)

and part or all of the cervix is removed and the stump is replaced in the vaginal cavity. This technique precludes the occurrence of hemorrhage from the uterine vessels, and insures the vagina and peritoneal cavity being closed tightly.⁴⁰ In the bitch, queen and sow a similar technique can be used, but the incision is circular and the uterine stump can be closed by a Connell suture followed by a Lembert stitch. In the bitch a dorsal episiotomy may be necessary in order to make the operation less difficult. In the bitch, queen and sow a laparotomy can be done, the prolapsed horn returned to the abdominal cavity, and an ovario-hysterectomy performed.

In the cow or ewe the most common technique recommended for amputation of the prolapsed uterus consists of making certain that neither the bladder nor any intestine is present in the prolapsed portion and then ligating that portion close to the vulva, using a strong ligature or preferably a soaped or oiled cord or fine rope tightened by two men pulling on opposite ends of the cord or rope. Three or 4 separate ligatures are firmly tied around the neck of the prolapsed portion of the uterus allowing 15 to 20 minutes to elapse between the application of each ligature. This is necessary as edema is always present in such cases, and the enclosing ligatures

must be tight enough so that when the uterus is removed 3 or 4 inches caudal to the ligatures the uterine vessels in the mesovarium will not withdraw into the abdominal cavity and cause fatal hemorrhage. Some veterinarians have successfully used a heavy elastic ligature made of long 2-inch-wide strips of rubber inner tube wrapped a number of times very tightly around the neck of the prolapsed portion in a manner similar to the cord method just described. After a lapse of 20 to 30 minutes to permit the edema to be forced from beneath the ligature, the uterus is amputated, leaving a fairly large stump to be replaced in the vagina. The ligatures or elastic tubing should be held in place by transfixing sutures through the enclosed vaginal wall. Following this operation the cow should be observed closely for evidence of shock, and saline solution, blood, glucocorticoids, and other stimulants should be administered at once. This is very important if the patient is to survive, as shock or hemorrhage may be fatal. The stump replaced in the vagina will slough in several weeks. It is usually advisable to administer parenteral antibiotics for 4 to 6 days.

Invagination of the Uterine Horn is occasionally noted in the cow and mare, but occurs only rarely in other species. In this condition the ovarian pole of the gravid

horn in the cow and usually the nongravid horn in the mare is everted but not far enough to be observed at the vulva. Ordinarily the invagination is completely within the uterus and is like an intestinal intussusception. It is more likely to occur during or after parturition and after replacement of a prolapsed uterus. It may be due to the pull or weight of the attached placenta on the ovarian pole of the uterus. Not infrequently it may be produced by traction on the fetal membranes at the time their removal is attempted. In a few cases the ovarian pole of the uterus may become incarcerated and necrotic with the cow showing symptoms of a septic metritis and peritonitis followed by death. In some mild cases the condition may correct itself spontaneously, while in others the invagination may progress until complete prolapse of the uterus occurs. This is another reason for careful examination of the uterus after relieving a dystocia.

The symptoms of an invaginated horn may be lacking, or there may be evidences of uneasiness, straining, or pain. In an occasional advanced case the invaginated portion of the horn may become necrotic; there may be symptoms of toxemia and septicemia; and a fetid, reddish-black vulvar discharge similar to that in a septic metritis may appear. On rectal palpation the enlarged uterine mass may feel like a large intussusception, and the mesovarium will be tense and tight. On vaginal examination if the hand can enter the uterus the invaginated horn is recognized as a dome-shaped, tumor-like mass projecting upward into the lumen of the uterus. This is noted most often in removal of an afterbirth in the cow when strong traction is placed on the placenta and the ovarian pole invaginates toward the cervix. In the mare this may also occur and in most cases involves the nongravid horn.

The prognosis is usually good unless the invaginated ovarian pole has been incarcerated by the contracting uterine muscle and becomes necrotic, in which case death usually occurs unless a hysterectomy is performed. The treatment of the condition in large animals consists of kneading the invaginated pole back into place with the fist, with piston-like shaking movements around the edge of the uterine lumen. Douching with 2 to 4 gallons of water may aid in replacing the invaginated pole. If one hand inserted in the rectum puts traction on the cranial portion of the broad ligament and the mesovarium attached to the invaginated pole, and the other hand pushes on the "tumor," this bimanual action may reduce the invagination. Ordinarily when the uterus is contracting strongly this condition cannot be relieved at that time. In cases where the invaginated horn cannot be replaced, when the animal's uterus is examined again in 3 to 6 hours it will be found that the condition often was cor-

rected spontaneously after the uterus relaxed. The attending veterinarian should closely follow and treat such cases of an invaginated uterine horn until the condition is corrected.

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METABOLIC DISEASES OF THE PUERPERAL PERIOD

Milk Fever, Parturient Paresis or Hypocalcemia is a metabolic nonfebrile disease of dairy cows usually four years of age or older, characterized by hypocalcemia occurring just before, during, or most often within 72 hours after parturition and the onset of lactation.¹⁹ Parturient hypocalcemia is an adaptation disease.¹¹ Although difficult to quantitate parturient hypocalcemia costs the dairy industry many millions of dollars each year.¹⁹ At the beginning of lactation when there is an increased demand for calcium, 2 to 5 times that of the gestation period, the cow is forced into a hypocalcemic state and parturient paresis ensues.^{11,16,19,20,21,23} With the onset of lactation an adequate increase in dietary calcium intake and

absorption to meet the body demands is essential. Inappetence frequently associated with parturition, together with the "lag period" of several days before bone tissue is activated to supply sufficient calcium retard the normal adaptation of the cow from the loss of calcium at the onset of parturition and lactation and results in a high incidence of parturient hypocalcemia and relapses following therapy.¹⁹

The blood serum calcium level drops from a normal of 8 to 12 mg. per 100 ml. to 3 to 7 mg., with symptoms of parturient paresis becoming progressively more pronounced as the calcium level declines. Hypocalcemic paresis is due to a depression of neuromuscular transmission of motor stimuli.⁶ Subclinical hypocalcemia, with calcium levels below 8 mg. per 100 ml. of serum may last for 11 to 32 hours in many parturient cows without paresis developing. Paralysis was usually associated with calcium levels below 5 mg. per 100 ml. serum.²⁰ Hypophosphatemia, hyper- or hypomagnesemia and hyperglycemia are other changes associated with parturient hypocalcemia.¹⁹ Parturient paresis is observed in all dairy breeds but most commonly in Jerseys. Recurrent attacks of milk fever may occur at subsequent parturitions.

The symptoms of parturient paresis are anorexia, cold extremities, lowering of the body temperature, stiff gait, staggering, incoordination, inability to rise, an S-curve in the neck, failure of the pupil to contract on stimulation by light, suppression of urination and defecation, constipation, slight tympany of the rumen, cessation of parturition if it develops during that period, coma, and finally death usually occurring in 6 to 24 hours if treatment is not instituted. Only rarely does spontaneous recovery occur in the paretic cow. With proper care and prompt handling the prognosis is good, and the mortality should be less than 2 to 3 percent in uncomplicated cases that do not injure themselves in attempting to rise. Prolonged recumbency in parturient hypocalcemia frequently results in pressure damage of ischemic necrosis of muscles and inflammation of sciatic and peroneal nerves leading to the downer cow syndrome and death.⁷ Early and prompt treatment of milk fever is necessary to avoid the latter syndrome especially in the larger heavier, often obese, cows of the Holstein breed. It has been demonstrated that 50 percent of normal healthy cows confined in recumbency for 6 to 12 hours developed extensive lesions leading to the downer cow syndrome and death or euthanasia.⁷

Treatment consists of administering 500 to 1000 ml. (depending on the size of the cow) of 20 percent calcium gluconate, one half of the amount injected intravenously and one half subcutaneously. In 100 cows recumbent with parturient hypocalcemia the overall relapse rate was 22

percent after treatment with calcium preparations either intravenously or intravenously and subcutaneously. The incidence of relapse was about 38 percent in the cows treated only intravenously while it was about 4 to 8 percent in the cows treated both intravenously and subcutaneously.⁸ In these latter cows the serum calcium levels 12 hours after treatment were significantly higher than the cows only treated intravenously. Reduced amounts of milk should be removed from the udder for 2 to 3 days. Complete emptying of the udder should be avoided if possible.

Udder insufflation to raise the plasma calcium concentration by reducing milk secretion and transferring calcium in the udder back into the circulation was reported upon.²¹ This technique did not induce hypercalcemia and was seldom followed by a relapse. Cotton-filtered compressed air from a cylinder introduced into the barrel of a syringe filled with an antibiotic udder infusion preparation to firmly distend the cow's udder and teats was used. Following treatment the teats were tied with a tape for several hours to hold in the compressed air. Since 1930 many attempts have been made to prevent parturient hypocalcemia by administering large amounts of vitamin D either orally or by injection. These studies have been recently reviewed.^{19b} Although various forms of vitamin D and D₃ will produce a temporary hypercalcemia, their toxicity and the timing of the administration of these products with parturition have created serious drawbacks to their practical widespread acceptance and use.^{19a} Recent preliminary studies on administering a large dose of a readily absorbed proprietary calcium product containing other trace minerals and vitamins immediately after calving has shown some promise in reducing the incidence of parturient hypocalcemia and retained placenta in dairy cows.⁹ Milk fever or hypocalcemia has been described in the ewe, doe and sow mainly in Europe. The symptoms are similar to those in cows.³

To prevent the occurrence of parturient paresis which may reach an incidence of 80 percent or more in the pluriparous cows in certain dairy herds, the total dietary calcium intake late in lactation and during the nonlactating period should be greatly reduced by removing legumes such as clover and alfalfa from the diet as well as common mineral supplements used for lactating cows which are usually high in calcium. This practice causes a slight hypocalcemia and increased secretion of parathyroid hormone. Timothy hay, straw and corn silage are low in calcium content and may be fed.^{13b,19} If too much of the corn silage is fed the cows may become overly fat resulting in the "fat cow syndrome" in which the cows are more susceptible to milk fever, ketosis, digestive dis-

orders as displaced abomasums, retained placentas and metritis, mastitis and foot problems. In certain areas and herds where some or all legume roughage must be fed, the addition of 2.5 to 5 percent monosodium phosphate to the grain ration, resulting in Ca:P ratio of 1:1 instead of a 3 to 7:1 may reduce the incidence of milk fever.^{5,13b,19} However low calcium diets, regardless of dietary phosphorus intake, prevent milk fever by the prepartal activation of both bone and intestinal tract.^{13b}

Ketosis or Acetonemia is only rarely observed prior to parturition in cows.^{3,13} It may occur the first 7 to 10 days after parturition but by far the greatest number of cases occur from 10 to 60 days after parturition. Ketosis in dairy cows is a lactation disorder, with elevated levels of ketones in the blood, urine and milk, associated with high milk production and a negative energy balance.¹⁹ It is estimated that clinical and subclinical ketosis costs U.S. dairymen about 150 million dollars a year. Three types of ketosis in cattle may develop:²⁴ (1) primary spontaneous ketosis which may have an hereditary predisposition, (2) primary nutritional, which is the most common and (3) secondary ketosis which occurs with reduced TDN intake due to metritis, displacement of the abomasum, traumatic gastritis and other diseases. Ketosis is characterized by hypoglycemia, ketonemia and ketonuria. The normal bovine blood levels of 40 to 60 mg. per 100 ml. of glucose drop to 40 to 18 mg. of glucose and the blood ketone levels rise from a norm of 2 to 15 mg. to 15 to 75 mg. per 100 ml. This condition is due basically to a reduced intake of nutrients, especially carbohydrates, in relation to the loss of energy by heavy lactation. Secondary conditions such as fatty changes in the liver may occur. There is a marked loss in weight due to the use of body fat, carbohydrates and proteins for milk and energy. The condition may develop in dairy cows at any age.

The symptoms observed are of two types, digestive and nervous. In the more common digestive type, the symptoms are anorexia, constipation, gradual drop in milk flow and rapid loss of weight. In the less common nervous type the symptoms are more severe, and depression is marked; various nervous symptoms such as trembling, nervousness and licking may be present; paresis is not uncommon, and anorexia and drop in milk flow are also observed. At times it may be difficult to differentiate between acetonemia and metritis following parturition, and both may be present. By testing the urine or milk with Ross reagent, the development of a definite purple color is usually indicative of ketosis. Inasmuch as very few animals die of ketosis, the prognosis is good; but the loss in milk production and body weight can be of great economic importance to the dairy farmer. The av-

erage incidence of ketosis in the United States is about 4 percent but in some high producing herds it may reach 20 to 50 percent. The condition is more common in the winter stabling period.

The treatment of ketosis in cattle consists of raising the blood sugar level for a period, thereby restoring the cow's appetite. Following the increased intake of additional nutrients, especially carbohydrates, the cow will recover and a relapse is unlikely. The preparations used to raise blood glucose levels include glucose solutions of 500 ml. to 1000 ml. of 40 percent glucose injected intravenously, or continuous, slow intravenous drip of several thousand ml. of 25 percent glucose. Sodium propionate, 1/3 to 3/4 lb. fed daily in small doses or given as a drench or a similar but more palatable product, propylene glycol administered orally in 200 to 500 ml. amounts daily increase propionic acid in the rumen which is absorbed and used by the cow in place of glucose. This conserves and raises the blood glucose level. Glucocorticoids injected intramuscularly raise blood glucose levels rapidly and also improve appetite and lower milk production for several days. ACTH, 200 to 600 I.U. injected intramuscularly stimulates production of the glucocorticoids by the adrenal glands and thus raises the level of blood sugar. Ten to 30 gms. daily of chloral hydrate in divided doses given orally also raises blood sugar levels. If metritis, mastitis or other infectious process due to bacteria is present the glucocorticoids should not be given or they should be accompanied by parenteral antibiotics. They are contraindicated in viral diseases. Relapses are likely to recur if the level and amounts of nutrients, especially carbohydrates, TDN or energy in the ration are not increased so that the cow will consume 1 lb. of 12- to 14-percent protein grain for 2-1/2 to 4 lbs. of milk produced, depending upon the quality and quantity of roughage. The level of energy intake must equal the work of milk production so that the cow maintains a positive energy balance and does not relapse into ketosis. As nutrition and management of present dairy cows are improved to reduce ketosis, the genetic increase in future milk production of cows will ensure this disease remains a problem.

Ketosis or Pregnancy Disease in Ewes is seen the last 2 to 4 weeks of pregnancy. Usually the dam is carrying twin or triplet fetuses. It is caused by a hypoglycemia produced by the rapid growth of the fetuses and insufficient intake of nutrients, especially carbohydrates in the ration.³ Ketosis is not due to an insufficiency of ACTH as hydrocortisone levels are elevated.¹⁰ The affected ewes are usually thin but ketosis may be observed in ewes in good condition. It is also predisposed by a lack of exercise. The liver shows fatty changes and the

ketone levels in the blood and urine are greatly elevated. In ewes the symptoms of ketosis are dullness, anorexia, paresis, or inability to rise without assistance, and nervous symptoms of mental derangement such as walking in a circle, pressing the head against some object, drawing the head backward and to one side. The nervous signs exhibited might be due to inability of nerve cells to utilize sugar.¹⁰ Urine obtained by a small catheter or by stopping respirations by squeezing the nose and mouth firmly shut can be tested by the Ross test, as in cattle, for the presence of ketones. In more advanced cases the fetuses die and if they are aborted promptly the ewe may recover. Ketosis may be differentiated from listeriosis by a lack of paresis of the lips or ears. In listeriosis the limbs are flaccid while in ketosis the limbs will resist flexion if upward pressure is applied to the toe. The course of the disease is 2 to 6 days. The prognosis is usually poor unless cases are diagnosed and treated early or abortion occurs before the ewe is severely affected. Treatment consists of any one or a combination of the following: the injection of 200 ml. of 40 percent glucose intravenously; administration of glucocorticoids or 50 to 100 I.U. of ACTH intramuscularly which may initiate premature parturition; an increase in the carbohydrate intake of 1/2 to 1 lb. of grain, 1/4 to 1/2 lb. of molasses daily per ewe or 2 ounces of propylene glycol 2 to 3 times a day. Sometimes valuable ewes which are severely affected can be saved by cesarean section; the fetuses are often dead. The glucocorticoids and estrogens have been used to cause or hasten parturition or abortion in ewes with severe ketosis. The disease may usually be prevented in the rest of the flock by increasing the grain ration or by feeding molasses and increasing the amount of exercise. Ketosis in goats is similar to that in ewes but is observed less commonly.

Grass Tetany, Lactation Tetany, Transport Tetany, "Wheat Poisoning" or Hypocalcemia, or Hypomagnesemia is a metabolic disease of beef and dairy cattle, and sheep and goats in Europe, especially those which are in advanced pregnancy or lactating heavily, grazing on lush, heavily fertilized grass or early wheat pastures or are transported or stressed in the puerperal or early lactation period. This disease complex is well-described.^{3,19} It occurs more commonly on certain types of soils and in certain regions. It is seen most often during the spring or fall months and less often during the summer months. Grass tetany is characterized by a hypocalcemia, occasionally a concurrent hypomagnesemia, or hypomagnesemia alone. It is caused by the excessive consumption of young lush grass on well-fertilized pastures. Some^{9a,17} believe that the high potassium or transaconitate and citric acid content in grass causes a loss of

calcium and magnesium from the body, accentuated in advanced pregnancy or during heavy lactation, when there is an increased drain on body calcium and magnesium. Hypomagnesemia may occur in stabled animals fed rations low in magnesium. The symptoms of grass tetany are similar to those of milk fever when a simple hypocalcemia with hyper- or normo-magnesemia is present. If, however, a hypomagnesemia is present with hypo- or normo-calcemia trismus, hyperesthesia, tachycardia, nystagmus, erect ears, tetany of the hind limbs, tremors, twitching of muscles that may progress into general spasms or convulsions, may be exhibited.¹⁷ Paresis is a common symptom. Unknown extrinsic or intrinsic factors apparently play a role in precipitating signs of hypomagnesemia when the serum levels of magnesium are low. A recent study indicates there may be a relationship between age, renal function, magnesium antagonists and parathyroid hormone in the etiology of hypomagnesemic tetany.^{9a} Decreases in magnesium levels in the cerebrospinal fluid are more closely associated with clinical signs of grass tetany than are serum magnesium levels. Thus grass tetany may be due to alterations of central nervous system function possibly brought on by vascular lesions and hemorrhagic edema characteristic of pathologic lesions of grass tetany.¹⁹ Often during the early stages of grass tetany the animal is excitable and may be aggressive. Some hypomagnesemic cows may act normally until handled when signs of tetany suddenly develop. This disease is more gradual in onset than is milk fever. The prognosis is usually good but sudden deaths are not uncommon if the condition isn't treated early.

The treatment consists of injecting 500 to 1000 ml. of a calcium-magnesium solution intravenously and subcutaneously in a divided dose, removing the animal from the grass pasture, feeding good alfalfa hay, and supplying a mixture of bone meal or dicalcium phosphate, and magnesium oxide, sulphate or carbonate, up to 60 to 120 gms. daily, free choice, in a molasses block or preferably in the grain ration. Since magnesium can't be stored in large amounts in the body, a nearly daily intake is necessary. Magnesium may be combined with the calcium gluconate or 200 to 500 ml. of a 10 to 25 percent solution of magnesium sulphate may be given subcutaneously. An outbreak of transport tetany or hypocalcemia was described in which a flock of ewes kept on a stubble field low in calcium was driven 9 miles to a new pasture. The ewes near parturition or in early lactation showed depression, stiff gait, high pulse and respiration rate and excessive salivation. Giving 150 ml. of 20 percent calcium gluconate subcutaneously resulted in recovery.¹

Tetany or Eclampsia in the Mare is rare but has been

described.³ Usually it occurs within several weeks after parturition, in a mare that has a normal foal, is lactating heavily, and is on a good, lush pasture. An attack may be precipitated by unusual handling, transport, or by a change in surroundings. It is probably a hypocalcemia similar to grass tetany in the cow or eclampsia in the bitch. In the early stages, symptoms of restlessness, rapid breathing, staring eyes, twitching, trembling and clonic spasms, especially of the diaphragm, are common. In later stages clonic spasms are followed by more tonic spasms, with trismus, marked restlessness, labored breathing, profuse sweating, and injected cyanotic mucous membranes. In advanced cases the animal is unable to stand. Tetany of most muscles is present; the animal becomes prostrate; convulsions are nearly continuous; and death results in 12 to 48 hours. The condition should be differentiated from tetanus. If treated promptly the prognosis should be good but deaths are not uncommon in untreated mares. Spontaneous recoveries have occurred at any time during the course of the disease. The treatment consists of intravenous injections of calcium gluconate and possibly the administration of narcotics such as chloral hydrate, sodium pentobarbital or heavy tranquilization.

Puerperal Tetany or Eclampsia in the bitch and queen is a metabolic disease characterized by hypocalcemia.^{2,26} It is seen in heavily lactating bitches during the first 3 weeks after parturition, although it may occur prior to, during, or up to 6 weeks after parturition.^{4,18} The serum calcium level drops from a normal of 9 to 12 mg. to 5 to 7 mg. per 100 ml. It may occur in all breeds but is seen most commonly in small or medium-sized bitches. The disease is characterized by rapid breathing, a dry mouth and sclera, restlessness, nervousness, and whining, followed by staggering, incoordination, stiffness of limbs, and an elevated body temperature. Later there is the development of symptoms of inability to rise, extended legs, excessive salivation, champing movements, dilated pupils, clonic and tonic spasms and convulsions, congested mucous membranes, labored respirations and a rapid, hard pulse. The prognosis is good if treatment is instituted. Spontaneous recoveries may occur. Treatment consists of administering sodium pentobarbital or 5 to 10 ml. of a 10 percent calcium gluconate solution intravenously, intraperitoneally or subcutaneously. Recurrence of the condition is more common following the use of calcium gluconate than of sodium pentobarbital. If the pups are old enough they should be weaned. The bitch and queen should be fed added amounts of calcium lactate or gluconate in the ration. The administration of corticosteroid therapy, 5 mg. prednisolone or 25 mg. hydrocortisone, daily will help prevent a relapse. If given

for a week or more the steroid therapy should be withdrawn gradually.¹² If the bitch has metritis, antibiotics should be given with the corticosteroids. If affected bitches are rebred the condition frequently recurs in the subsequent lactation period.² The disease is rare in the queen but symptoms and treatment are the same as in the bitch.¹⁰

Postparturient hemoglobinuria is an uncommon disease of high-producing, older dairy cows occurring 2 to 4 weeks after calving and characterized by hemoglobinemia, hemoglobinuria, and anemia.³ It is associated with rations deficient in phosphorus or rations high in rape, turnips, kale, beet pulp or cabbage. The affected cows show anorexia, weakness, dehydration, pale mucous membranes, rapid pulse and respiration, constipation and in the later severe stages, prostration and death after a course of 3 to 5 days. In mild cases or treated cases recovery occurs after several weeks. In severe cases there is a hypophosphatemia as low as 0.5 to 1.5 mg./100 ml. of serum; normal values are 4 to 6 mg./100 ml. Postparturient hemoglobinuria should be differentiated from leptospirosis and pyelonephritis. Treatment consists of blood transfusions to effect; the intravenous injection of phosphorus containing compounds and oral supplementation of the ration with monosodium phosphate or possibly bone meal or dicalcium phosphate especially if cruciferous plants are in the diet.³

Puerperal Metabolic Diseases

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Puerperal Infections, Uterine Infections and Diseases

Retained Placenta or Retention of the Afterbirth or Fetal Membranes is one of the most common conditions occurring in animals following parturition. It is observed chiefly in the cow and less commonly in the other domestic species.

Retained placenta in the cow. In physiological parturition the afterbirth of the cow falls away within 3 to 8 hours following calving. If the placenta is retained longer than 8 to 12 hours the condition is considered pathological.

Etiology. Retention of the fetal membranes is basically due to failure of the villi of the fetal cotyledon to detach themselves from the maternal crypts of the caruncle. After the fetus is expelled and the umbilical cord ruptures no blood is pumped into the fetal villi and they shrink in size. In the dam, uterine contractions continue and the large amount of blood formerly going to the uterus is markedly reduced. The maternal caruncles become smaller in size, due to a reduced blood supply, and the maternal crypts dilate. Although there is no muscle in the caruncle, during contractions of the uterine wall following parturition the shape of the caruncles may change from oval to round.² Detachment of fetal cotyledons from the maternal caruncle was much easier during these contraction waves than between them. The weight of the fetal membranes assist in their normal dropping away from the caruncles and the uterus. Other workers^{17,24,60} have stated that stimulating uterine contractions by the injection of oxytocin immediately after calving apparently lowered the number of retained placentas, by comparison with control cows not thus injected. In a small trial oxytocin, 40 IU every 20 to 30 minutes for up to 6 treatments, was given to cows judged unlikely to pass their fetal membranes with a reduction of the incidence of retained placenta by 50 percent.¹⁷ Separation of buffalo calves from the dams immediately after birth so that suckling could not stimulate the release of oxytocin from the posterior pituitary gland, resulted in 22.7 percent retention of the afterbirth in 189 calvings as compared with 4.9 percent retained placentas in 122 calvings on the same farms when suckling was allowed.⁶⁸ Stress could also have been associated with this high incidence of retained placenta.

On histologic examination of fetal cotyledons and maternal caruncles taken an average time of 4.75 hours after normal calving, degeneration and necrosis of the fetal villi and necrosis and degeneration of the epithelium of the maternal crypts were present, and the latter were filled with debris.³⁵ These findings in normal cows were essentially similar to those in cows having a retained placenta. Incomplete data showed little or no histologic differences between normal cotyledons and caruncles and those in which retained placenta developed. There were morphologically three types of retained placentas; one type was associated with abortion and premature birth with immature placentomes; the second type was associated with hyperemia and were few in number; and the

third and most common type was associated with small portions of necrotic epithelium between the chorionic villi and the cryptal walls.⁹ In retained placenta normal separation and loosening of the villi from the maternal crypts is interfered with and adhesions form. In easily removed placentas the loosening process comes about by autolysis of the chorionic villi. After several days leucocytes and bacteria were in the placentomes. Therefore placentitis was a secondary phenomenon. The incidence of retained placenta is high in births occurring several days before the expected date because the placenta has not undergone the degeneration necessary for normal detachment.⁸ Although there is as yet no definite information about the exact manner in which the fetal membranes are expelled or fall away from the caruncles, it is rather apparent that it is a complex process involving a reduction of blood supply followed by shrinking of both maternal and fetal placental structures, degenerative changes, and strong uterine contractions.

There is evidence to show that infections of the uterus during gestation may be a cause for retained placenta. Infectious agents, such as *Brucella abortus*, tuberculosis, *C. fetus* and various mold infections cause a placentitis and cotyledonitis resulting in abortion or pathological parturition at term with retention of the placenta. Sound evidence to minimize the importance of this general cause of retained placenta has been provided.² This author agrees that in the past too much emphasis has been placed on intrauterine infections during gestation as a cause for retained placentas. About 20 to 25 percent of 282 cases of retained placenta in one study²⁴ were infected with *Brucella abortus*, but these were also associated with abortions and premature births. The occurrence of many placental retentions in herds affected with *C. fetus* were reported. It was stated⁸ that 30 percent of all retained placentas in cattle in Germany were due to *Brucella abortus*. The author has observed many mold infections, due to *Aspergillus* or mucor molds, causing a marked cotyledonitis and severe retention of the fetal membranes. Examination of 2027 placentas revealed 121 with mold.⁷ Of these latter 73 percent were *Aspergillus*. Many infected placentas were not retained. Other diseases and organisms causing abortion or premature birth might also produce endometritis, placentitis, and retention of the fetal membranes by inflammatory reactions of the cotyledon and caruncle similar to lesions described in brucellosis.²⁸ As noted in Chapter V, under uterine involution, during or following parturition, bacteria from the caudal portions of the genital tract or the environment invade all uteri. The degree of contamination or numbers of invading bacteria, the type and virulence of the organisms and the immunity or re-

sistance of the dam determine the seriousness of the infection which may vary from a mild infection with a rapid recovery within a few days or weeks to a severe metritis, septicemia, toxemia and death in the same period.⁷⁰

The highest incidence of retained placenta, 69 percent, occurred in an experimental group of cattle on low levels of carotene intake.⁵⁶ The incidence could be correlated with the various feeding levels of carotene. In hyperkeratosis, and P.B.B. toxicity, in which vitamin A levels are very low, the incidence of retained placenta, metritis, and abortion is high. Probably vitamin A is necessary for maintaining the health and resistance of the epithelium of the uterus and placenta. Low vitamin A levels lead to the development of infections. A deficiency of minerals such as iodine and selenium has been reported to be a cause of retained placenta, but this requires further substantiation.⁴⁴ Premature calvings and calves with enlarged thyroid glands together with an increased incidence of retained placentas may occur in iodine deficient herds.^{16b} Numerous recent studies have been performed in cows to prevent retained placenta by the injection of vitamin E and selenium about a month before parturition.^{32,48,61,62} In Ohio and Kentucky this therapy proved effective in reducing the incidence of retained placenta but in Maryland, Virginia, New York, North Carolina, Nebraska and South Dakota it was ineffective. There were great variations in results between herds. Thus this therapy cannot be recommended with assurance of its value.

Retained placenta in 1610 Holstein parturitions was 50 percent higher in both cows and heifers with dystocia than in normal births, and 50 percent higher in calvings in which milk fever occurred than in calvings where no milk fever was present.⁵² Heat stress during the summer months, May through September, in Georgia increased the incidence of retained placenta and metritis from 12.2 to 24.0 percent. This was apparently related to a reduction in the length of gestation by 5.25 days in the cows with retained placenta compared to the cows calving during the cooler seasons.²⁰

In the cow, many abortions occurring after the fifth month of pregnancy are accompanied by retained placenta. In cattle calving 1 to 2 weeks prematurely, especially in twin pregnancy, retained placenta occurs in 30 to 50 percent of the animals. The ratio of retained placenta to abortions at different times of gestation was 1:7 at 121 to 150 days, 1:6 at 151 to 180 days, 1:3 at 181 to 210 days, 1:2.2 at 211 to 240 days and 1:1.7 at 241 to 250 days of gestation.⁴⁶ Practically no retained placentas occurred after abortions prior to 120 days and the incidence dropped to 1.5 percent of calvings between

271 and 280 days of gestation. Progesterone deficiency may cause the retention of the fetal membranes or indirectly cause it by predisposing to early parturition.⁴² It may be possible that some abortions, premature calvings, or retained placentas are due to a progesterone deficiency or a cortisol excess late in gestation. Profiles of hormone levels in cows with and without retained fetal membranes 12 hours after calving were not conclusive. Further studies in the week prior to calving are indicated as low estradiol and high progesterone levels on day 6 prepartum were associated with retained placenta.¹⁵ Inducing parturition 2 to 10 days before expected calving usually resulted in a 50 to 75 percent incidence of retained placenta. (See Chapter VI.)

Diseases causing uterine inertia or atony result in a high incidence of retention of the fetal membranes. These are: dropsy of the fetal membranes, uterine torsion, twinning, fetal giantism, primary or secondary uterine inertia, dystocia, and other pathological conditions. Retained placenta was observed in about 70 percent of dystocia cases due to uterine torsion and failure of cervical dilation, and in about 25 percent of dystocia cases due to over-size of a living fetus.¹⁸ An incidence of 8 percent retained placenta in normal births but a 55 percent incidence in abnormal deliveries such as twins, cesareans, fetotomies, dystocias and abortions was reported.^{66b} Failure of normal uterine involution was frequently associated with retained placenta. The pathological conditions causing these diseases or abnormal conditions resulting in uterine inertia—whether they be infectious, hereditary, nutritional, circulatory, or hormonal—also predispose to retention of the placenta. In a study of 7,387 calvings in one Holstein herd for a period of 25 years, the incidence of retained placenta averaged 10.5 percent and affected 38.6 percent of the 2607 cows. Retained placenta rose from 5.4 percent in primipara to nearly 25 percent at the ninth calving.²³ Elimination of brucellosis from the herd did not lower the incidence of retained placentas. Twins and abortions were associated with 37.7 percent of all retained placentas. Significantly more daughters from dams having retained placentas had retained placentas than daughters from dams not retaining their afterbirth. Retained placentas were more common following the birth of single male calves, 56 percent vs. a 51.6 percent herd average. Twin births in which two males or one male was present also had a higher rate of retention. It was concluded²³ that retained placenta is not entirely caused by previous pathological conditions, a theory strongly supported by others.^{69b} Retained placentas were more common during February through April in the northern hemisphere.^{16a, 23}

Retention of the fetal membranes is less common in

beef breeds than in dairy breeds confined in stables for long periods. The incidence of retained placenta varies widely from herd to herd at various times. Retained placentas in 6.4 percent of 450 parturitions that included only brucellosis-free cows and births of living, single calves were reported.¹² An incidence of 8.3 percent in 431 calvings in British herds in which brucellosis was either absent or quiescent was recorded.³⁵ The incidence in Hannover, Germany, was 4 to 5 percent.² In over 24,000 calves in Israel, a 5.08 percent incidence of retained placenta in single births and a 99 percent incidence in twin births, for a total over all incidence of 8.4 percent was recorded.⁶ In New Zealand the incidence of retained placenta was 1.96 percent in over 36,000 dairy cattle kept at pasture the year around.⁴⁶ In comparison with stabled herds it may indicate that exercise, less stress, more vitamin A and a less contaminated environment is conducive to a low incidence of retained placenta. The incidence of retained placenta in herds infected with active brucellosis, in cows producing twins, or in cows aborting due to other causes is high, probably from 30 to 50 percent or more. Once retention of the afterbirth occurred in a cow, there was about a 20 percent chance of it recurring again.²³

It has been repeatedly observed by the author that in a certain year a high incidence of retained placentas 30 to 80 percent, would develop in a dairy herd that formerly had relatively few cases, 2 to 8 percent. Once retained placentas started nearly every cow calving thereafter would be affected and/or develop postpartum metritis. These herds were free of the common enzootic infections of reproduction that cause abortion such as brucellosis, vibriosis, leptospirosis, IBR-IPV and mold infections. The affected cows were calving in the same barn and in many instances in the same calving stalls in frequent succession. When there was an hiatus of several months or more when no cows calved or when cows were calving on pasture away from the barn, the incidence of retained placenta and metritis dropped dramatically to the low levels of former years even when calving was again resumed in the barn or calving stalls at a later date. This pattern of retained placentas and postpartum infection closely resembles that seen in calf scours and the metritis-mastitis-agalactia syndrome in sows. In fact the author has observed severe outbreaks of virulent scours in the newborn associated with a high incidence of retained placentas and metritis in the dams in the same herds. From these observations the author has hypothesized that these severe enzootic outbreaks of retained placentas and secondary metritis were due to certain highly virulent organisms of *Streptococcus dysgalactiae*, *E. coli*, *Staphylococcus*, *Pseudomonas aeruginosa*, *C. py-*

ogenes and/or other organisms which developed in these barns or calving stalls infecting the genital tract of the parturient cow at the time of calving and causing an acute metritis, uterine inertia, retained placenta and then secondary placentitis and metritis. As long as cows are calving in frequent succession in such an environment the infection continues from one cow to the next. When a period of several months or more elapses between cows calving in such an environment the infection dies out on the premises. Since it is difficult to thoroughly disinfect a barn or even most calving stalls a possible alternative is to remove the parturient cow from this environment to a clean noninfected one for calving. This is difficult on most farms and farmers are reluctant to go to this inconvenience even if suitable noninfected calving stalls or areas can be improvised. On affected farms where the author has secured the cooperation of the farmer to follow this regimen of removing the parturient cow from the infected environment for 5 to 10 days before and after calving whether by placing the cow in a noninfected or noncontaminated separate barn, lot, shed or stall or by putting the cow on pasture, the results have been very gratifying with a marked drop to normal in the incidence of retained placenta and postpartum metritis. Because of the adverse effects on reproduction and milk production the veterinarian should not hesitate to strongly recommend this often troublesome chore upon the farmer. With the increased size of many dairy herds and the trend toward "zero" pasture and the confinement of cows in barnyards and freestall housing, the author foresees the continuation of such serious problems unless management and housing designs develop so that calving stalls can be built isolated from each other and of such construction that lends itself to thorough disinfection as has been necessary for continuous farrowing operations to develop in the swine industry. There is evidence in England, Sweden and the U.S.A. that bedding cows on sawdust is more conducive to coliform mastitis, calf scours and retained placenta and post-partum metritis than bedding the animals on straw. For those of my readers who are reluctant to accept the hypothesis that acute uterine infections resulting in retained placentas and metritis can develop in the few hours between the onset of parturition and the normal time of expulsion of the placenta they should note the very short period needed for the development of acute bovine mastitis, calf septicemia and acute mastitis in sows.

The morbid anatomy of retained placenta may vary from slight evidence of disease to severe lesions. According to the location of the inflammatory reactions in the uterus, placentitis may be classified as apical, cervical or diffuse. The nongravid horn may or may not be

involved when the placenta in the gravid horn is retained. The degree of placentitis in the nongravid horn is usually not as severe as in the gravid horn since the placentomes are smaller and less complex. The degree of placentitis may vary from a mild peripheral type of necrosis involving only the villi to a severe necrosis involving the entire cotyledon and a part or all of the caruncle.

If the placentitis developed prior to calving or abortion, the allantois chorion may be edematous, necrotic or leathery, or hemorrhagic. Uterine "sand" and old or fresh clotted blood may be present. Often a reddish-brown to yellow exudate is found in the utero-chorionic space. Adventitious placentae may vary from a few small areas to nearly complete involvement of the entire endometrium of one or both horns. In mold infections the cotyledon is usually very large and swollen. Uterine and placental disease may occasionally cause fetal disease or anoxia that results in the presence of fetal meconium in the amniotic fluid, staining the fetus. In most cases of retained placenta the calf appears quite normal.

The symptoms of retained placenta are usually obvious, a portion of the fetal membranes hang from the vulva 12 hours or more following abortion, normal parturition, or dystocia. Occasionally the fetal membranes do not hang from the vulva but are entirely within the vagina or uterus. In the treatment of herds severely affected with genital disease close observation of the cow to observe when the fetal membranes were dropped is recommended.^{69b} Examination of the fetal membranes can be made to be certain they are completely expelled and no portion remains in the uterus. If they are not expelled normally the uterus should be examined manually per vaginam in 24 to 36 hours. After 48 hours it is usually difficult or impossible to insert the hand into the uterus if no fetal membranes are within the cervix. The presence of the membranes lying in the cervix tends to retard contraction of that organ. After a dystocia the placentomes may be felt; if they are very swollen, hard, firm, inflamed, or congested, the placenta will be retained. If the placentomes are soft and pliable the cow will often drop the afterbirth within a few hours.

About 75 to 80 percent of cows with retention of the fetal membranes show no marked illness. About 50 to 60 percent may exhibit slight to moderate illness by a temporary reduction in appetite or milk flow.² About 20 to 25 percent may exhibit moderate to severe symptoms of metritis and septic metritis as shown in some cases by anorexia, depression, elevation of body temperature, increase in pulse rate, decrease in milk flow, and loss of weight. These percentages may differ in herds depending upon the severity of the infections causing the

secondary metritis. In severely affected animals retained placenta may be associated with or complicated by other diseases such as: mastitis, septic metritis with perimetritis or peritonitis, severe straining, necrotic vaginitis, parturient paresis, and acetonemia. The bacteriological picture of the uterus in cases of retained placenta was similar to that of a uterus with delayed involution or atony without retained placenta.² First the *Streptococci dysgalactiae* and the staphylococci appear, and later the diptheroids, *Corynebacterium pyogenes*, coliform, and anaerobic bacteria may be found. In retained placenta the white blood cell picture showed a slight to marked shift to the left. In uncomplicated cases a lymphocytosis developed. In more severe metritis cases a definite leucopenia occurred.⁴³ The total number of white blood cells usually do not increase markedly. After 24 hours the placenta begins to macerate and a fetid, putrid odor develops. The afterbirth may fall away anytime within 24 hours to 14 days, depending upon the severity of the disease and possibly the type of treatment used. In most cows with retained placenta the cervix contracts after 48 to 72 hours, so that it may be difficult to insert the hand through the cervix. This contraction takes place sooner if no fetal membranes are present in the cervix.

Prognosis. The mortality rate in retention of the fetal membranes should not exceed 1 to 2 percent in uncomplicated cases.² In retained placenta cases a mortality rate of 4 percent: emaciation, infertility, or unprofitableness in 20 percent, a short duration of the disease with temporary irregularities of milk production and fertility in 50 to 60 percent, and nearly undisturbed puerperium in 15 to 25 percent was reported.² Another study²⁴ reviewed a substantial number of cases of retained placenta treated by various means in the Ambulatory Clinic of the New York State Veterinary College from 1920 to 1941. During the years 1920 to 1928, 755 cases were treated by early or late removal, and much douching, with a mortality rate of 4.2 percent. During 1928 to 1934, 1109 cases were treated by removal at 72 hours, with little or no douching, with a mortality rate of 2.8 percent. From 1934 to 1941, 1680 cases were treated with late removal, 72 hours or more, no douching and liberal use of sulfanilamide, with a mortality rate of 1.1 percent. In this same clinic, from 1943 to 1953, 3742 cases of retained placenta were treated by late removal, 72 hours or longer, no douching, and the use of sulfonamides and antibiotics, if necessary, with a mortality rate of 1.3 percent. This latter figure included cases in which septic metritis, mastitis, peritonitis, and other conditions were complications which undoubtedly contributed to or caused the fatalities. A very interesting study⁵¹ was conducted of 44 cases of retained placenta in 2 herds totaling 125

animals in which no manual removal of the placenta was attempted during a period of 3 years. These herds were free of brucellosis and tuberculosis. No treatment was given to any cows with the exception of 4 that became quite ill. In these 4 cows proflavine and saline solutions were introduced into the uterus but probably had no influence on the course of the disease. Of the 44 cows 81.8 percent had calved at term, 18.2 percent had aborted, and 16 percent had twins. The placentas were retained from 2 to 11 days, an average of 6.8 days before dropping away naturally. During the first two weeks after calving the appetite was good in 31.8 percent, fair in 54.5 percent, and poor in 13.6 percent. Body weight remained normal in 88.6 percent. Lactation was good in 29.5 percent, fair in 63.6 percent and poor in 6.8 percent. When the 44 cows that had untreated retained placentas were compared with 44 cows in the same herds calving normally without retained placenta there was no significant difference in the numbers of cows in the two groups having to be sold because of sterility, abortion, or delayed conception. In these two herds no cows were bred back until 90 to 150 days after calving.⁵¹

The effect of retained placentas on subsequent fertility is important to consider, as delayed involution and chronic endometritis following retention of the membranes is common. Apparently after 2 to 3 months and a number of estrous periods most cattle having a retained placenta eliminate the infection and the uterus becomes normal. In 71 abnormal calvings the postpartum interval from calving to complete uterine involution averaged 52 days or only 5 days longer than in 252 cows that calved normally.¹³ If the owner desired to breed the cow before 90 days after the abnormal calving, examination of the uterus to determine if it was completely involuted was recommended. About 20 percent of cows retaining their placenta at one calving had another retention at subsequent parturitions. Young cows having a retained placenta averaged one less calving than cows the same age not affected with retained placenta.²³ Cows not having genital disorders such as chronic metritis following retained placentas were nearly as fertile as normal cows but there was a 30 to 50 percent greater probability that genital disorders would occur in affected cows. The nonreturn rate to first service before 60 days postpartum was 28.2 percent in cows with retained placenta and 50.3 percent for cows without a retained placenta; after 60 days the comparable percentages were 52.2 percent and 64.0 percent. When "nonreturn" cows after service were checked to diagnose pregnancy they found 10.6 percent of 592 cows with retained placenta at their previous calving were not pregnant while only 5.4 percent of 19,173 cows with no retention were not pregnant.⁴⁶ Following

retained placenta in some cows, permanent sterility results, due to pyometra, perimetritis, salpingitis, ovaritis, severe damage to the endometrium, or other causes related to the retention. In most of the animals affected with retention of the fetal membranes the major loss is an economic one of a slight to moderate loss of milk and a slight to moderate delay in the involution of the uterus and subsequent conception.

In 100 dairy cows calving within a 4-month period,^{12b} 27 percent had retained fetal membranes of which only two-thirds were noted within 24 hours after parturition. Thirty-four percent of the cows had postpartum metritis of which 76.5 percent were secondary to other postpartum problems, mainly retained fetal membranes. Despite several types of local and systemic antibiotic therapy given within 24 hours of parturition to problem cows, 76 percent developed a secondary metritis compared to 12 percent of the untreated normal-calving cows. Delayed uterine involution at 30 days postpartum was more than twice as common in the cows with metritis than in the normal-calving cows. This recent study and review^{12b} confirms earlier reports on the lack of information on the incidence, causes and therapeutic procedures to prevent and treat herds and cows with postpartum uterine disease problems.

Treatment. After reviewing the literature on bovine retained placenta and listening to many veterinarians describe their methods of treatment, the author has been amazed and impressed by the infinite number and variety of techniques employed, the drugs and hormones recommended, and the time lapse between parturition and the attempted removal of the placenta. With so many varied techniques and products being used, one is forced to recognize the fact that probably no treatment would be necessary in handling most cases of retention of the fetal membranes. This has been demonstrated.⁵¹ In England and in Europe there is an increasing volume of opinion in favor of not making any manual attempt to detach the fetal placenta from the maternal caruncles.² No matter how carefully the operation is performed some injury to the endometrium may result, and the risk of toxemia and septicemia is thereby increased.

Presently the author conservatively recommends that all cows having a retained placenta 12 hours after calving be given a parenteral antibiotic injection that may be repeated. Since the colostrum milk is discarded this therapy causes no economic hardship and the cow is significantly protected against a serious uterine or systemic infection. It is optional with the owner and veterinarian whether the placenta is removed manually.

A clean, manual examination of the uterus can be made. The operator should wear a surgical rubber glove and

long sleeve on one arm and a surgical glove on the other to protect himself from brucellosis or an infection of the arm or hand. Disposable plastic gloves and sleeves of good quality are more sanitary and practical than rubber gloves and sleeves. He should wear rubber coveralls or an apron and boots that may be easily cleaned and disinfected after the operation. The perineal region of the cow should be carefully cleaned and washed with soap, water, and mild antiseptic, and kept clean during the operation. To keep the cow, especially one with loose feces, from either defecating frequently or straining, epidural anesthesia may be used. A plentiful supply of clean water is essential. The cow's tail should be held out of the way by an assistant or tied with a tail rope over the back to one of its fore legs. The free part of the fetal membranes should be drawn through the cervix, thereby reducing the amount of membranes in the uterus and aiding its drainage. If the fetal membranes fall away readily from the caruncles they should be removed. If much fluid is present in the uterus it should be siphoned off by a sterile soft rubber horse catheter or stomach tube held in the fist to keep the fetal membranes from plugging the end of the tube. The siphon may be started by filling the rubber tube with water and holding it pinched off as it is introduced. Douching the uterus is contraindicated when membranes are present as it is difficult to remove the fluid completely. Another method of removing this excess fluid is to use large swabs of absorbent cotton and gently wipe the uterus free of exudate.²⁴ Large amounts of fetid reddish watery fluid in the uterus is usually accompanied by signs of toxemia, depression, and anorexia.

Manual removal of a retained placenta in the dairy cow is practiced by most veterinarians because the diseased, macerating fetal membranes are serving no good purpose and the farmer desires and expects the veterinarian to remove this unsightly fetid mass from the genital tract. In most cases the fetal membranes have not macerated sufficiently for easy removal before 48 hours after parturition. Although in some cases enough autolysis has occurred so the villi separate readily from the crypts and removal may be accomplished easily as early as 12 to 24 hours after calving. The best time for removal of the placenta was reported to be 24 to 48 hours after parturition.^{6,64} These easily removed fetal membranes would probably have dropped away without aid within another 24 to 48 hours. It has been the practice of the author and many other veterinarians not to examine or treat retained placenta until 72 hours after parturition unless the cow develops anorexia, an elevated temperature or other symptoms of septicemia. At this time the uterus has contracted in most cases so the apex of the horn may be

reached. The cervix is usually still sufficiently open to allow passage of the hand and arm without resultant trauma. When removal is attempted at 72 hours after parturition the uterus has developed a protective barrier to the infection and there is less chance of a septicemia or toxemia occurring than there would be if removal is attempted earlier. At whatever time the placenta is removed this should be done gently and quickly within 5 to 20 minutes, in a clean manner, and with as few withdrawals and reintroductions of the arm as possible. The use of epidural anesthesia controls straining and defecation and makes possible a cleaner, more hygienic, and gentler operation. If the operation cannot be performed in a gentle manner, with as little interference as possible with nature's processes, the fetal membranes should be left alone even though the cervix may contract so that on subsequent visits by the veterinarian the hand cannot be inserted into the uterus. If this happens it is best not to attempt dilation of the cervix, as it is difficult or nearly impossible to do so without severe trauma. The membranes should be allowed to fall away naturally, or gentle traction on the fetal membranes will remove them after the maternal caruncles and fetal cotyledons have separated from the uterine wall by autolysis. Even if the membranes or a portion of them macerate and are absorbed in the uterus this is better than severely traumatizing the cervix in attempts to dilate it.

It has been observed by the author and others that if the placenta is allowed to drop away of its own accord, or if it is gently withdrawn from the uterus even 10 to 12 days after parturition, involution of the uterus occurs sooner, and cessation of uterine discharge ceases more quickly than when the placenta is removed in a rough manner and portions are left in the uterus. In a study of 632 cows with retained placenta a conservative systemic treatment with sulfonamides orally and intravenously resulted in higher subsequent fertility than a more "radical" treatment with manual removal and various local intrauterine treatments.²⁹ The uterus containing a retained placenta may be compared with a large abscess in which the necrotic core has not separated from the surrounding tissues. The surgical procedures governing the handling of an abscess should also govern the handling of the infected uterus. Conservative treatment is indicated and essential.

The veterinarian should have the courage of his convictions in handling these cases, inasmuch as traumatizing the uterus by attempting to remove the placenta when removal is difficult or impossible results in either immediate septicemia with a marked drop in milk and appetite, elevation of temperature, loss of weight and possible death, or else a prolonged period of convalescence

during which time shreds of placenta and exudate are expelled from the uterus, pyometra or chronic metritis develops, or protracted or even permanent infertility may result from a uterine abscess, perimetritis, salpingitis or severe endometritis. If in order to avoid traumatizing the uterus or leaving placental shreds and fragments in the uterus a veterinarian refuses to remove a placenta that is not ready to be separated from the maternal caruncles, and explains to the owner his reasons for the decision, this may prevent criticism by a client who formerly has been accustomed to having the placenta "taken" on the first and only call in all cases of retained placenta.

Manual removal of the placenta is contraindicated in cows with an elevated body temperature, above 103° F. and in cows or heifers suffering from severe necrotic vaginitis. In the former a septicemia and toxemia are already present and would be aggravated by manual manipulation of the placentomes. Administration of antibiotics parenterally and locally, or sulfonamides orally or intravenously in cows showing toxic symptoms is indicated for a period of several days before removal is attempted. Removal of the placenta particularly in heifers having necrotic vaginitis and vulvitis with a small, dry, swollen genital canal may make the vaginitis and vulvitis worse and may increase straining that is probably already present. Since it has been proved that most cows suffering from retained placenta need no treatment, and the others only parenteral treatment with antibiotics or parenteral and oral treatment with sulfonamides to control septicemia, the removal of the placenta from a cow with an elevated temperature, vaginitis, septic metritis or possibly other diseases, such as acute mastitis and traumatic gastritis, is contraindicated. Removing the placenta in an incomplete, rough, insanitary manner is always inadvisable.

Occasionally when the union between the cotyledons and caruncles is very firm and most of the caruncle becomes necrotic and sloughs, it may be 10 to 15 days before the macerating placenta and cotyledons can be removed. If the fetal membranes are removed prematurely by traction or improper manual removal, thereby leaving the fetal cotyledon on the necrotic maternal caruncle, these necrotic caruncles and cotyledons may become dry and inspissated and remain as a foreign body in the uterus for 3 to 8 weeks or longer. When found several weeks after parturition, they may be removed by injections of estrogens to relax and dilate the cervix and contract the uterus together with gentle massage of the uterus per rectum. A rubber douche tube may be used as a siphon and by suction on the caruncles by the siphon tube they may be coaxed and withdrawn through the cervix. If left in the uterus these may eventually macerate,

but recovery is prolonged and chronic metritis, pyometra and sterility usually occur.

In removing the placenta manually the third or fourth days after parturition, or earlier if the placenta can be removed easily, the hand is inserted between the endometrium and chorion in the intercotyledonary space and the individual fetal cotyledon and its caruncle are grasped gently, squeezed, and with the thumb and forefinger the two structures are gently separated by a rolling, pushing, squeezing motion. This may be aided by traction with the other hand on the adjacent portions of the fetal membranes as the separation is completed. The cotyledons in the cervical area of the uterus are removed from the caruncles first and then by traction with the outside hand the placenta is pulled out and tension maintained as the cotyledons in the middle portion of the horn and the non-gravid horn are removed. The ovarian pole may be difficult to reach. Sometimes traction on the placenta will pull the apex of the horn nearer the cervix and thus aid removal. It is highly desirable to remove all of the fetal membranes and not leave remnants in the uterus to act as foci of infection as these must be expelled or macerate before recovery can take place.^{69b} The blood vessels of the placenta are among the last portions of the placenta to macerate. If the entire placenta cannot be removed, it is better to insert a few capsules, tablets, or a solution of antibiotic and revisit the cow in one to three days, or let the placenta fall away naturally.

The layman's practices of tying a weight on the placenta or of cutting the placenta off close to the vulva are not desirable. First, the weight frequently causes the cow to strain and causes premature and incomplete breaking away of the afterbirth, leaving a part of it still in the uterus. In rare cases this weight may cause invagination of the uterine horn. Removing the placenta close to the vulva in order to prevent the cow from swinging it against the milker is likely to result in the placenta dropping back into the uterus followed by early closure of the cervix. The afterbirth may remain in the uterus long after it has separated from the caruncles, because the weight of the placenta hanging from the vulva is not present to draw it out. If the placenta is dragging on the ground it should be cut off at the level of the hocks to prevent its being stepped on and torn away from the uterus.

Hormones have been widely used in the treatment of retained placenta. The use of oxytocin has been mentioned as being of possible value in preventing retained placenta when given shortly after the expulsion of the fetus or after dystocia operations. In dystocia, besides aiding in the expulsion of the fetal membranes, oxytocin may prevent prolapse of the uterus. It is advisable to inject 3 to 5 ml., 30 to 50 units, immediately after calving. One to

3 further subcutaneous injections of 2 to 3 ml. of oxytocin at 1- to 2-hour intervals may be given. Occasionally injections of oxytocin precipitate milk fever in cows with subclinical hypocalcemia. The oral administration of a proprietary calcium product containing trace minerals and vitamins within a few hours after calving reduced the incidence of milk fever and also reduced the incidence of retained placenta by about 50 percent.¹⁹ Further studies on the administration of oxytocin and calcium to cows failing to drop their fetal membranes soon after calving is indicated as there is a close association between milk fever and retained placenta. Oxytocin is of questionable value after 24 to 48 hours after calving.

The estrogens have been widely used in the past in the treatment of retained placenta. Stilbestrol or estradiol has little or no effect on the rate of separation of the fetal cotyledons and maternal caruncles. Estrogens do, however, exert a definite action on the uterus by increasing its tone and muscular activity, stimulating the flow of mucus, increasing the circulation, and relaxing the cervix. These facts, together with the reports^{10,57} that the uterus is better able to control or overcome infection during estrus or when treated with estrogens, show the logic of using this hormone in the treatment of retained placenta. Presently estrogens are rarely used to treat retained placenta or metritis in dairy cows because of the ban on their use in dairy cows in the U.S. to prevent their presence in milk. Some cases of uterine atony associated with retained placenta may greatly benefit from the injection of calcium gluconate especially if a subclinical hypocalcemia is the cause of the uterine atony.²⁴ Following the injection of calcium during the first day after calving the afterbirth is often expelled within several hours. If the uterus is severely diseased and atonic the uterine wall may be incapable of responding to the injections of hormones. In recent years many veterinarians have used 1 to 3 mg of ergonovine or a similar product developed from ergot that produce a more prolonged rate of uterine contraction than doses of oxytocin. The results are equivocal.

A wide range of antiseptics have been used locally to control the bacterial flora in the treatment of retained placenta and the uterus following removal of the retained fetal membranes. These early drugs consisted of such products as charcoal, boric acid, acriflavine, bismuth subnitrate, bismuth formic iodide, bismuth thymol iodide, chlorine preparations, iodine in oil, silver oxide, bismuth formic iodide in oil, chlorophyll and bismuth and iodoform in oil (Bipp). This latter product imparted an odor to the milk that prohibited its use in dairy cattle. Various products containing sodium perborate have been

advocated to aid in the removal and treatment of retained placenta. On contact with tissue debris these products release much gas and cause foaming similar to that resulting from the use of hydrogen peroxide. These products are slightly irritating and probably should not be used in the uterus if the cervix is contracted. Because of their effect on tissue debris a number of enzyme products containing urea, yeast, pepsin, and papain have been advocated. It is doubtful if these varied preparations greatly alter the course of the disease.

Sulphonamides have been used locally in the uterus and have been approved by some veterinarians. Other veterinarians indicate that these drugs are rather insoluble, especially in a tablet form, and tend to settle in the apex of the horn and are of questionable value. Penicillin, streptomycin and tyrothricin have been used widely in the past in the local treatment of retained placenta. The former is usually quickly inactivated by penicillinase produced by the infective organisms in the uterus and the latter is rather irritating in large amounts. In recent years 1 to 3 gm. of the broad-range antibiotics such as oxytetracycline (Terramycin), Chlortetracycline (Aureomycin), Tetracycline, Furacin and others have been used locally in cases of retention of the fetal membranes. For immediate response these are used as an infusion in 200 to 1,000 ml. of saline or warm water. The boluses or powder produce a slightly slower response. These appear to be the first products used locally that definitely alter the course of the infection. The rate of putrefaction and lysis is greatly reduced. The usual fetid odor is largely eliminated. The retained membranes may tend to remain attached to the caruncles in the uterus for a slightly longer period. The use of these products in a case of septic metritis usually eliminates the local infection quite promptly and if used early, 24 to 36 hours after calving or as soon as the temperature becomes elevated or other signs of illness develop they usually bring about a prompt regression of the illness. After the use of **Aureomycin** in the uterus in 612 cows with retained placenta, only 2 cows developed acute metritis.^{5,27} In 31 cows with retained placenta manual removal was not attempted and 0.5 gm of **Aureomycin** was placed in the uterus every 1 to 2 days until the afterbirth dropped away. This took 2 to 10 days, with an average of 5.2 days. Subsequent conception rates were excellent.²² It was recommended that manual removal not be attempted. After treating 508 cows with retained placenta in various ways, one study reported that cows receiving local tetracycline intrauterine medication had a lower conception rate than those cows not receiving medication. If medication was initiated it was better to wait until 36 hours or more postpartum. Whether the retained membranes were removed or al-

lowed to drop away had no effect on subsequent fertility.⁴⁶ Conception rate on the first service was higher, 70 percent vs 40 to 50 percent, and days from parturition to conception were lower, 86 vs 91 to 110 days, in cows treated with intrauterine oxytetracycline within 72 hours of calving and the placenta was not removed than in cows receiving no medication. Removal of the placenta definitely lowered the conception rate at first service.⁴

Observations and reports have shown that hormones, sulfonamides, and antibiotics are rapidly absorbed from the uterus into the bloodstream.^{8b,50b} This systemic effect is further reason for the topical use in the uterus of these easily administered products. If large doses of antibiotics are placed locally in the uterus, the milk from treated cows should not be put in the supply for about 72 hours.

If symptoms of septic metritis develop with retention of the fetal membranes, sulfonamides administered orally, or sulfonamides and/or antibiotics administered parenterally are of great value along with supportive treatment with saline and glucose solutions, and possibly blood transfusions intravenously as described under the treatment of septic metritis. As in horses, laminitis often accompanies septic uterine infections in cattle but is not as obvious. The local treatment of the uterus should be very gentle and manual removal of the placenta should not be attempted. In rare cases a severe anaerobe or necrophorus infection may invade the uterus and these infections are usually fatal. In Europe in areas where anaerobe infections are common antiserum is usually administered after a dystocia. If severe straining is present with retained fetal membranes, epidural anesthesia should be given and the uterus and birth canal carefully and gently examined. In most cases the straining is due to a severe vulvitis or vaginitis, and these should be treated. Rarely it may be due to an invagination of the uterine horn. Tenesmus may also be associated with rabies in endemic areas.

It is recommended that all cows affected with retained placenta be examined 20 to 30 days after removal of the afterbirth to determine if involution of the uterus is proceeding normally and that postpartum metritis or pyometra is not present. If this is not done the cow may fail to show estrum and 90 days or more after parturition the disease condition will be diagnosed too late to prevent a serious delay in conception. Permanent sterility may result. The owner should be advised that many older cows affected with retained placenta should not be bred until 90 days after parturition. This time interval is usually necessary for proper involution and overcoming of the infection in the diseased uterus. In valuable cows the involution and return of the uterus to normal can be checked by periodic examinations during this period. If

the uterus is completely involuted, no genital discharge is present and regular estrous cycles are occurring, cows with a history of retained placenta at the last parturition may be bred at 60 days postpartum with a good conception rate. All cattle having a persistent mucopurulent discharge from the vulva following retained placenta should be reexamined and treated.

Retained Placenta in the Mare is probably less common, from 2 to 10 percent, and more variable than in the cow.⁶⁷ Probably the same factors responsible for retention of the placenta in the cow also are present in the mare. The infection most commonly observed in association with retained placenta in the mare is *Streptococcus zooepidemicus* but many other organisms may be involved, especially the gram-negative ones that produce endotoxins and histamines. Many genital infections in the mare are related to vulvar defects leading to pneumovagina. In some mares air and infectious organisms may be aspirated through the cervix into the uterus during the act of windsucking. Infection also gains entrance to the uterus following foaling, when the mare gets up. A rush of air often fills the dilated genital tract and uterus and the membranes draw debris from the bedding into the uterus. Straw and shavings or sawdust are the worst offenders. It was suggested that Tartan or a similar covering over a cushioning material would greatly reduce uterine infection after foaling.³ If the mare remains recumbent after foaling, until the placenta is about ready to drop away, the uterus is more contracted and less air is aspirated. The rush of contaminated air into the uterus after foaling might play an immediate role in the retention of the afterbirth. Retained placenta more commonly accompanied the large draft foals than the light horse foals.³³ A lack of breeding and foaling hygiene might possibly explain why some draft mares are more likely to have retained placenta than are Thoroughbred mares. Repeated breedings during one heat period or the breeding of infected mares or infected stallions may cause retained placenta. Placentas weighing over 14 lbs. in light mares were usually associated with infections of the uterus, and a chorion that was characterized by necrotic areas and edema.³³ Retained placenta is probably less common in mares because of the simple, diffuse type of placentation and the strong uterine contractions aiding the separation of the villi from their maternal crypts and expelling the detached membranes. It is interesting that the physiologically expelled placentas of most mares, as in cows, are inverted. This apparently is due to the fact that the allantois chorion first separates from the rapidly contracting apices of the uterine horns and passes into the birth canal before it is separated from the uterine body. Retained placenta in the mare is likely to occur

following abortion and prolonged gestation.^{69b} Probably the causes for retention of the afterbirth in the mare are infection, uterine inertia and other factors similar to those affecting cattle.

Symptoms. Physiologically the equine fetal membranes are expelled within 0.5 to 3 hours after parturition but it is fairly common to have the fetal membranes not drop away until 8 to 12 or more hours later without any observable symptoms of illness. Strong uterine contractions in the mare after foaling and just before expulsion of the placenta are often accompanied by signs of abdominal pain, recumbency, and colic.² The mares that retain their afterbirths exhibit no such pains and appear normal, content, eat and drink, and suckle their foals. Slow expulsion of the placenta may be due to uterine inertia or exhaustion following expulsion of the fetus. The onset of delayed expulsion is indicated by the mare developing colicky pains followed by the dropping away of the membranes in from 10 to 20 minutes. In a few nervous mares it is necessary to tie up or cut off the hanging retained placenta so that it will not frighten the mare into kicking and otherwise possibly injuring the foal. In dystocia the fetal membranes may be detached and wrapped around the fetus. The rapid separation of the fetal membranes probably accounts for the early death of the fetus in many equine dystocias. Retained fetal membranes can usually be observed hanging from the vulva. Occasionally the placenta may partially fall away and the apex or tip of the placenta will remain in the nongravid horn especially if the apex is thickened and edematous. The weight of the placenta or the mare stepping on it may rip it away, leaving the tip of the nongravid horn in the uterus. This piece of placenta may act as a focus of infection often resulting in a severe metritis and secondary laminitis the third to seventh day after foaling. The afterbirth of each mare should be carefully examined after it falls away, to make certain no portion of the placenta remains in the uterus. Most cases of laminitis occurring after foaling are due to metritis often associated with a portion of the placenta being retained and floating in a uterus filled with fetid fluid. Uterine invagination or intussusception, usually of the nongravid horn into the uterine body, may accompany retention of the fetal membranes in the mare but it is seldom of a serious nature.^{25,30} The prognosis of retained placenta in the mare is usually good.

Treatment. It is generally recommended that removal of the placenta in the mare not be attempted for at least 12 hours after foaling.^{8a,30,33} No treatment until 20 to 24 hours after foaling was recommended if the mare continues to eat, has a normal temperature and the pulse rate remains normal. With retained placenta it is common

practice to administer 2 to 4 ml. of oxytocin, 20 to 40 units, subcutaneously or intramuscularly every 2 to 3 hours starting the fourth to twelfth hour after foaling. Vandeplassche⁶⁷ recommended the administration of 40 to 60 units of oxytocin in 500 to 1000 ml of saline by slow intravenous drip over a period of 1 to 2 hours as a more physiologic way in which to give the hormone. This treatment is successful in about 75 percent of the cases.⁶⁷ The placenta was often passed during this period. It may be necessary to administer a tranquilizer to control mild colic and pain associated with the uterine contractions produced. In most cases the afterbirth drops away within a few hours or before 24 hours have elapsed. Injections of **Aureomycin**, tetracycline or Terramycin, 1 to 3 mg. per pound of body weight daily, intravenously; or the intramuscular injection of 3 to 6 million units of aqueous penicillin daily and 5 gm. of streptomycin twice daily may be indicated to control infection for 2 to 4 days.

After 12 to 24 hours postpartum the veterinarian, in a scrupulously clean manner, should administer a tranquilizer, bandage or have the tail held out of the way and scrub the perineum of the mare with soap and water. His hand and arm enclosed in a sterile surgical glove and sleeve is inserted into the birth canal and the allantois chorion is grasped. By means of gentle traction and twisting on the fetal membranes to form a "rope," uniform traction may be applied to the fetal membranes as the hand is very gently forced between the endometrium and chorion in the places where it is still attached. It should be recognized that any direct manipulation of the endometrium may be damaging to it. The entire placenta, including the tips of the horns, should be carefully removed. If necessary, examine the placenta after removal to be certain that the removal is complete. A more conservative and gentle approach, which has much to recommend it, consists of inserting the hand inside the allantois chorion and gently massaging it away from the endometrium.⁵⁹ If removal does not occur promptly, supportive treatment should be given and the mare reexamined and treated 4 to 12 hours later.

Another method to remove an equine retained placenta without manual intervention has recently been described.¹⁴ After preparing the mare as described above the gloved hand enters the vagina and gently draws the chorioallantois out of the vulva. The torn ends of the cervical star portion are gathered together and a stomach tube is placed through the opening into the allantoic cavity. Two to 3 gallons of warm dilute povidone iodine solution, 4 ounces/gallon, are slowly pumped into the cavity to distend it. The hand around the membranes and tube prevent this solution from escaping. The distended

uterus stimulates the mare to attempt to expel the solution. These efforts may be augmented by the injection of 40 IU of oxytocin. The exposed fetal membrane is held and the solution is squeezed back into the uterus as the chorioallantois is slowly released. This is repeated frequently. It usually takes about 15 to 20 minutes for the complete release of the placenta which comes out intact including even the microvilli of the chorioallantois.

In one mare the author observed retained fetal membranes that remained firmly adherent to the endometrium for 72 hours without any adverse effect on the mare. Older local treatment consisted of inserting into the uterus a pint of oil. It is probable that the more stable but soluble broad-range antibiotics of the tetracycline and furacin groups would be of greater value in the local treatment of the uterus in mares, as in cows. Intrauterine therapy may be continued daily or every other day for 2 to 4 days until the uterus is well-involuted and the infection is largely overcome. It is highly desirable to administer tetanus antitoxin and probably oxytocin to a mare following removal of a retained placenta. Temporary skin clips or sutures may be placed in the upper two-thirds of the vulvar lips within several hours after foaling if the afterbirth has not been dropped and even after removal of a retained placenta in the mare to prevent aspiration of air into the genital tract.²⁵ At present douching of the uterus after removal of a retained placenta is considered a questionable practice although former workers advocated the general use of this technique. If the uterus is filled with fetid fluid this should be removed by siphoning through a sterile rubber tube. The danger of laminitis should always be considered. Ice packs should be placed on the feet and antibiotics given locally and parenterally until uterine infection subsides. Antihistamines and phenylbutazone might also be administered. Some advocate the use of stilbestrol, 30 to 60 mg., or estradiol, 3 to 6 mg., and ergonovine, 1 to 3 mg., intramuscularly daily for several injections. Large repeated doses of the glucocorticoids should not be given these mares.

Retained Placenta in the Ewe and Doe is handled in a manner similar to that in the cow except that removal from inside the uterus is seldom possible. If signs of elevated temperature, anorexia, and depression indicative of septic metritis are exhibited, parenteral injections of antibiotics, estrogens, oxytocin and antihistamines are recommended. Manual treatment is limited to occasional gentle traction on the hanging portion of the membranes. Some veterinarians introduce a broad-range antibiotic capsule or tablet used for enteric infections in calves into the uterus after carefully cleansing the ex-

ternal genitalia. The placenta usually drops away within 2 to 7 days.

Retained Placenta in the Sow is uncommon. It is usually impossible to determine if retention has occurred except by the symptoms of septic metritis, prostration, and a prolonged purulent vulvar discharge containing placental shreds. This condition has been reported² as a cause of fatal metritis, however this has rarely if ever been reported in the United States. Since retained placenta is most likely to occur after a dystocia with prolonged labor it would be advisable in these cases to save the expelled fetal membranes, count the umbilical cords, and to give oxytocin 1 to 3 ml., after relieving the dystocia. When septic metritis does occur because of a retained placenta, administration of stilbestrol, 10 to 20 mg. and the daily injection of intramuscular forms of antibiotics, such as 3,000,000 units of aqueous or oily preparations of penicillin, 1 to 2 gms. of streptomycin or 1 gm of intramuscular **Terramycin**, tetracycline, or **Aureomycin** are indicated. Intrauterine infusions of broad range antibiotics have been used by some veterinarians. A sterile AI catheter or a horse catheter may be used. The value of this type of therapy in the postpartum sow has not been proven. Good nursing is essential.

Retained Placenta in the Bitch and Queen is uncommon. It is seen most often in toy breeds in which dystocia or prolonged labor has occurred. In any such suspected case parenteral antibiotics should be administered at once and continued for several weeks. If the placenta is not expelled in 12 to 24 hours an acute metritis may result and unless it is treated early or a hysterectomy performed promptly, it usually is fatal in 4 to 5 days due to a necrosis of the uterine wall in the region of the placental attachments and peritonitis. Once toxic symptoms have developed in septic metritis in bitches due to retained placenta, the prognosis should be very guarded. The presence of a dark green vulvar discharge more than 12 hours after parturition is a symptom of retention of fetal membranes. If retained placenta occurs during whelping or is noticed within the first day afterwards, the retained membranes may be gently withdrawn from the birth canal and uterus with the finger. A pair of forceps padded with gauze or cotton may be rotated in the genital tract to wind up the membranes and remove them. In the small bitch the uterus might be palpated and massaged over the retained membrane to help to force the latter through the cervix. This might be repeated in several hours if unsuccessful initially.² In toy bitches after whelping and especially after dystocia a small dose of 1/2 to 1 cc., 10 to 20 units, of oxytocin may prevent retained placenta. If the bitch is valuable an attendant could watch her during whelping and save the

placentas to make certain all are expelled. If septic metritis is present, with a vulvar discharge, elevated temperature, rapid pulse, and anorexia the prognosis is guarded and treatment with antibiotics parenterally, as well as supportive treatment similar to that in other animals, should be given. Careful infusion of a small amount, 30 ml., broad-range antibiotic solution into the uterus might be indicated with a small soft rubber catheter. Injections of oxytocin may be of value. Supportive therapy with fluids is desirable. Laparo-hysterectomy might be considered but should be performed early.

Septic Metritis Following Parturition may occur with or without retention of the fetal membranes and is observed usually within 1 to 10 days after parturition in all species. The etiology of septic metritis is probably similar to that of retention of the fetal membranes. It usually is associated with a uterine atony or inertia. Highly pathogenic types of organisms are present in the uterus and they or their toxins are absorbed into the circulation, producing severe general symptoms associated with septicemia, endotoxemia, and pyemia. The organisms most commonly present are coliform organisms, **Coryn. pyogenes**, hemolytic staphylococci, **Ps. aeruginosa**, proteus, hemolytic streptococci, and in rare cases clostridia. These severe infections are characterized by a fetid, red, watery uterine fluid that is very toxic and depressing to the animal. This condition usually follows emphysema of the fetus, severe torsion of the uterus with the presence of a dead and possibly emphysematous fetus, and other conditions associated with a uterine inertia such as dropsy of the fetal membranes, fetal anasarca, fetal gigantism, twinning, peritonitis due to traumatic gastritis and retention of the fetal membranes. In many cases it may follow rough improper removal of a retained placenta. Probably most veterinarians in large animal practice can cite several instances in which septic metritis and even death followed the injudicious removal of a retained placenta in a cow when the owner insisted upon its being removed. Septic metritis may follow a prolonged dystocia especially if a difficult fetotomy operation has been performed. It may follow a prolapsed uterus or invagination of the tip of the uterine horn associated with trauma and infection of the endometrium. Occasionally it may result by extension from a necrotic vaginitis. It may occur in all species through the introduction of infection by unsanitary practices during the relief of dystocia or removal of a retained placenta. In bitches and sows it may occur from neglect at the time of parturition or trauma to the uterus with forceps, or accidentally allowing one or more placentas or fetuses to remain in the uterus and macerate. The use of cortisone without antibiotics by farmers soon after calving for the treatment

of ketosis may favor metritis.⁵⁵

The symptoms of septic metritis following parturition are very similar in all species of animals. Retention of the fetal membranes is frequently observed; in the cow the placentomes are usually greatly swollen and the fetal cotyledons firmly attached to the maternal caruncles. In the mare a piece of the placenta, often a portion from the nongravid horn, is retained and found in the body or nongravid horn of the uterus. The animals exhibit anorexia and dullness. The pulse is rapid, in the cow from 80 to 120 per minute, and usually weak. The body temperature in the cow may be elevated during the early phase of the disease. In advanced cases the cow's temperature may be either normal or subnormal. The latter condition usually occurs shortly before death of the animal. The cow is less apt to show a prolonged elevation of body temperature than are the other animals. The animal will shiver and its extremities are cold. The respirations are rapid and shallow; the eyes may be sunken; the hair coat is rough; and there is a rapid loss of weight. In severe cases there is a marked atony of the digestive tract. The feces may be hard and firm or may be black, oily, fetid, and liquid in character especially in the cow. A marked drop in milk flow or agalactia occurs in all species and the newborn will exhibit signs of malnutrition or starvation. There is usually a reddish, watery, fetid discharge from the vulva. The genital passageways are likely to be swollen and inflamed. Straining may be present or absent before the examination but during or after the examination it is generally present. In many cases of septic metritis with secondary enteritis in the cow, a rectal examination, especially if not performed gently, results in straining or tenesmus. The tenesmus may be very persistent and is definitely undesirable and exhausting to the cow. Rectal examinations should usually be confined to cows with no evidence of rectal irritation or enteritis. In some cows having septic metritis without a retained placenta the cervix may be quite contracted. Vaginal examination may reveal a normal vagina and clear, or only slightly cloudy, vaginal mucus, yet the uterine contents may be toxic and fetid, and occasionally toxic enough to cause death. The uterus in nearly all cases is atonic or flaccid. The walls are usually thin and in some cases, especially in bitches and queens, may be very friable or even necrotic, especially the placental sites. Peritonitis may be present due to extension of the infection through the uterine wall with symptoms of abdominal tenderness or soreness, abdominal distension, slight to moderate tympany of the rumen due to atony of the digestive tract, an arched back, stiff, slow gait, and tense abdominal muscles. The cow may exhibit a characteristic expiratory grunt due to the peritonitis.

Perimetritis or peritoneal involvement with the uterine infection may occur naturally or be produced by heroic or too vigorous treatment of a severely infected and inflamed uterus. Rectal examination on these cases in cows may reveal early fibrin deposition and adhesions present between the uterus and the adjacent abdominal viscera. If this is found, the operator should terminate the examination at once, or the peritonitis and adhesions may be made worse, leading to severe peritonitis, abscess involvement of the adjacent structures, marked adhesions around the uterus, broad ligaments, ovaries and oviducts, or even death. Arthritic symptoms, with swelling and stiffness of the joints, particularly the hock, fetlock and knee joints, may occur especially in the cow, ewe and sow. Acute laminitis in all large animals may also be present making the animal reluctant to rise and stand. The animal may be very weak, staggering, or prostrate and show symptoms of paresis and inability to rise. Since under these conditions the extremities are usually cold, this disease in the cow may easily be confused with milk fever. A mild to strong reaction to the Ross test for the presence of ketones may develop on testing the urine of cattle with septic metritis. This may be due to ketosis as a complication of the disease but more often it is caused by the severe anorexia. The blood count usually develops a marked shift to the left, together with a marked drop in the total white blood cell level during the early stages of the condition. During the recovery stage the white blood cell count shifts to the right, with a leukocytosis developing. Occasionally secondary complications of pneumonia, and laminitis in the mare, cow, sow, and ewe, and in all species pyemia with arthritis, liver, brain, or lung abscesses or endocarditis or myocarditis may develop especially if the condition is prolonged. Rough removal of the placenta, or lacerations of the endometrium encountered in prolapse of the uterus may allow organisms to localize in the uterine wall and cause an abscess.

A careful differentiation should be made between septic metritis and other conditions, such as traumatic gastritis, gastroenteritis, hemorrhagic septicemia pneumonia, parturient paresis, laminitis, and mastitis which may cause paraplegia, reluctance or inability to stand and illness at parturition. The course of septic metritis usually lasts from 2 to 6 days, with recovery or death occurring within that time. In the cow a prolonged course may extend over a period of from 1 to 2 weeks. The prognosis may be guarded to poor in many cases unless treatment is begun early before the uterus is severely damaged, peritonitis develops and the animal becomes extremely toxic. Failure to respond to treatment, persistent straining or complications such as mastitis and

pneumonia tend to make the prognosis grave. The prognosis for the future breeding life of the animal may be poor in severe cases as well as in cases of perimetritis, ovaritis or abscesses of the uterine wall. If recovery occurs conception may be delayed due to severe chronic metritis.

The treatment of septic metritis should be conservative. Massage and douching of the uterus, attempts to remove the retained fetal membranes should seldom if ever be performed in cases of septic metritis, or the animal's condition may become critical. Septicemia and toxemia should be overcome before these manipulative procedures are used. In early cases oxytocin, 30 to 50 I.U. in large animals or 10 to 30 I.U. in small animals may be of some value in producing tonus in the atonic uterus. Usually if the condition is severe hormones are of questionable or no value. If the uterus is filled with a large amount of fetid fluid this should be gently siphoned off. Siphoning the uterus in large animals should be done very carefully with a sterile soft rubber hose or horse catheter since the uterine wall may be very friable and easily ruptured. In the mare and bitch, if a portion of the placenta is lying in the uterus it should be removed in as gentle a manner as possible. One to 3 gm. of the broad-range tetracycline derivatives such as **Aureomycin**, **Terramycin**, tetracycline or furacin placed in the bovine or equine uterus in a solution or in a readily soluble form may be of great value in controlling the infection locally and even systemically by absorption from the uterus.⁵⁵ Antibiotics and possibly sulfonamide therapy are indicated parenterally. The antibiotics such as procaine penicillin, 3,000 to 6,000 units per pound of body weight daily and streptomycin, 5 gms. per 1,000 pounds twice daily, intramuscularly; Terramycin, or tetracycline intravenously; or in large animals except the horse; intramuscularly, at a rate of 1 to 3 mg. or more per pound of body weight, daily, are of definite value. The older sulphonamides given orally, or intravenously, may be used alone or with other antibiotics. Other supportive therapy such as saline and glucose solutions, and blood may be administered daily. Calcium gluconate seems of value especially in the early cases and may increase the tone of the uterus, but large doses given too rapidly to toxic cattle may cause death. **Pyribenzamine** or other antihistamines may be of value. Forced feeding may be helpful. Good nursing in a suitable stall or other equally comfortable environment is essential. If possible the large animal should be on green pasture each day or provided with fresh-cut green feed and with whole oats or other coarse feeds to tempt and encourage it to eat. If straining is present epidural anesthesia should be used to control it until the cause of the condition is determined

and corrected. A drop in pulse rate, an increase in appetite, an improvement in the tone of the uterine wall, a change in the exudate from a watery to a mucoid consistency are all favorable symptoms indicating that the animal is responding to therapy. Treatment should be continued until the animal has safely recovered and septic symptoms have subsided. This should take place before actively treating the uterus and removing the retained fetal membranes in the cow. It may be advisable to let the afterbirth drop away. In the mare septic metritis is more likely to cause laminitis, than in the cow, ewe or sow.

The application of ice packs to the mare's hooves, antihistamines and phenylbutazone, are indicated as preventive therapy in septic metritis. Laminitis may also follow metritis in the cow, ewe, and sow but is usually less severe and may be unnoticed until months later when deformity of the hooves becomes evident.

Postpuerperal Metritis may be observed from the time of parturition to 2 to 8 weeks or more postpartum in all species. It may persist as a chronic metritis for months or occasionally pyometra with anestrus and persistence of the corpus luteum may occur in the cow. There are no septic or general symptoms of illness accompanying this metritis. In most cases there is a reddish-brown or grey, mucopurulent, occasionally fetid discharge from the vulva. Later a creamy-yellow or grey discharge from the uterus and vulva usually mats the hair on the tail and buttocks. The condition is probably caused by many of the bacteria, especially **C. pyogenes**, that cause a retained placenta or septic metritis but either the infection is milder or the animal's resistance and the tone of the uterus are better. It may follow the development of infection in the uterine lochia during involution of the uterus. It may occur following retention of the fetal membranes or a necrotic piece of membrane or caruncle that has remained in the uterus. Occasionally it may be associated with a piece of the fetus, such as a hoof, left in the uterus and which has become a focus of infection. In mares it may follow a vulvar tear or laceration after foaling which causes persistent penumovagina and chronic metritis. Usually a cervicitis and vaginitis accompany the metritis, as by extension the infection from the uterus involves these structures. Rectal examination in cases of postpuerperal metritis reveals a larger than normal uterus undergoing a delayed involution. Uterine tone is fair but the uterine wall is thick and heavy. There may be from one-half pint to several gallons of mucopurulent material in the uterus of large animals. Vaginal examination may reveal some of this pus lying in the vagina. As late as two weeks after parturition the cervix in the cow with metritis is usually relaxed and dilated enough to admit

one finger. The uterine exudate is mucoid in character rather than watery as in septic metritis. Since postpuerperal metritis usually follows a retained placenta the veterinarian will find it advisable to reexamine valuable cows or mares 2 to 5 weeks after a parturition associated with retention of the placenta and treat the metritis and delayed involution of the uterus if they are present. In valuable cows a routine genital examination is usually performed in 3 to 5 weeks after parturition, even though retained placenta did not occur, to make certain that involution of the uterus is normal and that metritis is not present. There is evidence in mares and cows that probably 100 percent of parturient animals have infectious organisms invade the uterus for a short period of several days or more after expulsion of the fetus. At the time of the first estrus, at 5 to 12 days in the mare and 12 to 18 days in most cows, these infections are overcome and eliminated. In animals in which the first estrus is delayed or in animals failing to eliminate the infection, the infection persists as a mild to moderate metritis. With each subsequent estrous period more of these mild metritis or endometritis cases recover.^{59,70}

The prognosis in most of these cases is good. Many animals would recover without treatment but recovery time might be prolonged and conception delayed. Neglected postpuerperal metritis may progress into pyometra, chronic endometritis or cervicitis, and delayed or permanent infertility may result.

Treatment of these cases should start early, and repeated examinations and treatment at 1- to 3-week intervals may be indicated. Douching of the vagina of the cow with a gallon of hot, 120 to 130° F., mild antiseptic solution of chlorine, a soapy antiseptic, dilute **Lysol**, or other mild antiseptic 2 to 3 times a week stimulates uterine contractions, and washes the purulent exudate from the vagina. Intrauterine douching should be done gently, using only a soft rubber catheter, so that the endometrium is not traumatized. The exudate is thinned by the introduction of small amounts of a mild antiseptic solution, and then removed by siphoning. If the exudate is very thick, an enzyme like streptococcic dornase or pancreatic trypsin may be used to thin it and thus make it easier to siphon out. The recommendation in most of these cases is to avoid vigorous massage of the uterus or the removal of the corpora lutea in cows, since otherwise adhesions and perimetritis or ovaritis may develop. If the uterus is massaged this should be done gently. Antibiotics, and other antiseptics, such as 1 to 5 ml. of Lugol's solution or 10 to 20 ml. of **Betadine** in 100 ml. of saline or water, may be introduced into the uterus for local treatment of the infection. Large or prolonged doses of estrogen should be avoided lest cystic ovaries or the

transfer of infection through the oviducts with ovaritis and adhesions result. Estrogens should not be used in the dairy cow. Presently the prostaglandins such as F_{2a} or prostaglandin analogues are used to evacuate the uterus when a corpus luteum is present. Breeding of the animal should be delayed until the uterus and cervix are normal and 2 to 3 normal estrous periods have elapsed. Most affected cows should not be bred until 90 days or more after parturition although some may be normal and be bred at 60 to 80 days (See Metritis and Endometritis, Chapter XIII). In bitches, queens, and sows parenteral treatment of postpuerperal infections with courses of antibiotics and oxytocic agents are indicated to assist recovery. In rare cases laparotomy and hysterotomy with douching and infusing of the uterus with antiseptics and antibiotics might be undertaken.²¹ The mare may be treated similar to the cow except irritating infusions should not be used. If the mare or cow develops pneumovagina the Caslick operation should be performed. Because of the long period between lambing and breeding most ewes recover from postpuerperal metritis without treatment.

Lactation Failure, Hypogalactia or Agalactia, Mastitis-Metritis Agalactia (MMA) Syndrome of Sows is a heterogeneous disease complex with many possible causes. In this regard it resembles the postparturient paraplegic or downer syndrome in cows. Based on exhaustive reviews of this disease syndrome,^{40,68b} the name MMA is probably a misnomer. Much research on this syndrome over the past 20 years has shown that metritis is not a contributing factor in most cases and mastitis is not always a contributing factor. This syndrome of lactation failure affects 10 to 15 percent of sows farrowing in the midwest and is a contributing cause for the loss of 20 percent of the baby pigs due to starvation, hypoglycemia, overlaying and pig scours.

Lactation failure syndrome appears to be contagious but cannot be produced experimentally with regularity. The general categories of causes can be classified under infectious agents, managerial deficiencies related to nutrition, housing and stress, endocrine imbalances and possibly heredity for lactational ability.^{11,40,53,58,65,66a,68b}

E. coli and **Klebsiella** are commonly associated with mastitis and lactation failure. The latter organism has been associated with wood products used as bedding as in cattle. As with cattle, damp contaminated farrowing crates or houses can result in "bacteria-build-up" and be a cause for mastitis.^{68b} Endotoxins from these gram-negative organisms when injected into postparturient sows produce symptoms of the syndrome. These endotoxins may come from the mammary glands or the digestive tract. In the latter they may be associated with underfeeding, overfeeding or altered feeding practices with constipation.

Other bacterial agents have been associated with the agalactia syndrome including **Streptococci**, **Aerobacter**, **Citrobacter**, **Actinobacillus**, **Clostridia**, **Pseudomonas**, **Proteus**, **Mycoplasma** and **Staphylococcus**.

Endocrine studies of sows with lactation failure have revealed an elevated estrogen level 48 hours post partum in hypogalactic sows compared to normal sows. Serum prolactin levels were much lower than normal sows post-farrowing. Plasma cortisol levels were higher and thyroxine values were lower in affected sows. Evidence was presented of altered oxytocin release, increased engorgement of the udder and reduced ability to maintain blood glucose levels in affected sows.⁴⁰ Further correlation of these studies with management practices, infectious processes and heredity are needed to explain the pathogenesis of this multifaceted syndrome.

Overfeeding of the preparturient sow especially with finely ground feed and underfeeding causing hypoglycemia have been associated with this syndrome. But extensive studies have not revealed or demonstrated any uniform fault or deficiency in feeding practices. In fact the disease was observed with all commonly used feeding systems. Although selenium deficiency and hypocalcemia have been reported as possible causes for this syndrome, the evidence is not conclusive. Exercise on pasture during gestation is highly desirable. Sows that are susceptible to this lactation failure syndrome have been reported. It is possible that selection for lowered back fat and increased growth rate may favor the development of strains hereditarily susceptible to this disease.

On necropsy examination of affected sows, mastitis limited to a few areas of certain glands was found in 65 percent of the sows.⁴⁰ A mild metritis was present in 3 of 18 affected sows. Although all these above predisposing factors may be categorized as stress factors, further studies are needed to elucidate the complex interplay of the various causative etiologies.^{68b}

The clinical signs of lactation failure syndrome include: depression, anorexia, elevated body temperature, increased respiratory and heart rates, infrequent defecation, reluctance to rise and to allow nursing. These signs occur within 1 to 3 days after farrowing. Signs of mastitis may be evident or lactation failure can occur without systemic involvement of the sow. The pigs show signs of discontent by excessive running around and vocalizing. They become gaunt, weak and emaciated and are often crushed by the sow who is irritable and gets up and down frequently.

Treatment consists of providing feed for the malnourished piglets until milk flow is re-established in the affected sow or gilt. This can be done by placing piglets

with other recently farrowed piglets on another sow or feeding baby pig formula (SPF-Lac, Borden) or a formula of one quart cow's milk, one ounce white syrup or honey and one ounce of cream or corn oil. Piglets should be fed fresh warm formula every 1 to 3 hours for the first several weeks in amounts of about 10 percent of their body weight daily. Piglets should be left with the sow so as she returns to milk they may suckle.

The affected sow or gilt should be given oxytocin 30 to 50 I.U. at 3 to 4 hour intervals along with broad-spectrum antibiotics and possibly glucocorticoids to combat the endotoxin. Some veterinarians also give the sow estradiol and promazine tranquilizers. Preventive procedures should be directed at reducing stress. Avoid sudden changes in feeding and management. Handle sows quietly. House to avoid overheating and excessive humidity. Place sows in the farrowing house early enough so they become accustomed to it. Feed balanced coarse-textured mildly laxative grain ration with bran or beet pulp at a rate of 2 to 3 lbs. twice a day. Keep sows lean, don't let sows get overly fat.^{2,65} Feeds containing estrogenic mycotoxins should be avoided.⁴⁹ A daily exercise period during the periparturient period is desirable. Farrowing houses should be thoroughly cleaned and disinfected and allowed to stand empty for 1 to 2 months between farrowings and farrowing periods in a house should be limited to 3 to 4 weeks to avoid "bacteria build-up." Vigorous culling of affected sows is recommended. There is some evidence that lactation failure might be decreased by using prostaglandins to induce parturition after day 111 of gestation (See Chapter VI). Feeding high levels of antibiotics for a week before and after farrowing or the use of polyvalent autogenous vaccines to control infections have not proven to be uniformly of value.^{53,68b}

Agalactia in sows and mares associated with the ingestion of ergot or ergot-like alkaloids or mycotoxins (fescue) has been reported.^{1,38} This should be considered in a differential diagnosis in dams showing no systemic clinical signs other than agalactia along with a more excitable temperament. The active principal of ergot from the grain may be transmitted through the milk to the piglets resulting in gangrene of the ears and tails. In mares on certain fescue pastures in Missouri an increased incidence of agalactia was reported as a serious problem.

Postpartum metritis syndrome in cattle was described in 1963³¹ and has been seen with increasing frequency in many dairy herds in the Northeast especially as herd numbers increase and as production rises. It is becoming a serious problem especially in the free-stall herds with over 100 cows and where the cows never are placed on pasture. There are many similarities between

this postparturient syndrome in cattle and the postparturient agalactia in swine.

The postparturient metritis syndrome in cattle herds is characterized by a high incidence of retained placenta and subsequent metritis. Even in cows and heifers in which retained placenta does not occur, a postpartum metritis will develop. A few cases of metritis may exhibit septic symptoms but nearly 100 percent of the cows that calve during the Fall and Winter stabling season will exhibit a chronic metritis with a persistent yellowish discharge of pus that lasts for several months, a delayed involution of the uterus, a lowered conception rate and a calving interval that is increased from about 13 months to 15 to 17 months. Often an abnormally long period of anestrus follows calving. A few cases develop a persistent pyometra. In the early stages of the infection a wide variety of organisms are cultured but after several months *C. pyogenes* is the principal organism found. Economic loss is due mainly to delayed conception and culling because of infertility.

From his studies the author agrees that the postparturient metritis syndrome is principally a problem of sanitation in the barn, the free stalls, the exercise yards, and especially the calving stalls.³¹ In many instances calvings and postpartum involution of the uterus are normal for a period of a month or more at the start of the calving season. Then after one or two cases of retained placenta and metritis occur nearly every cow that freshens in these barns and calving stalls becomes infected (See Retained Placenta in Cows). In some herds with this problem nearly every calf born in these infected calving stalls will develop scours and die unless prophylactic antibiotic treatment is given as soon as the calf is born. Sometimes the owners in treating the cows prophylactically by placing antibiotics into the uterus may spread the virulent infection that has been established in the barn and calving stalls. Frequently this may only occur in a herd for one year. When the cows are turned to pasture or when a period of 2 to 3 months passes with no cows calving the infection will disappear. In large herds calving the year around the condition may remain a problem for years. If dry cows and pregnant heifers are removed from the herd and kept separate from the herd, calve at pasture or calve in a clean, noninfected environment and kept there for about 7 to 10 days this metritis syndrome will stop. To solve this problem some farmers have built portable 10' x 10' calving stalls that can be thoroughly disinfected between calvings and can be moved to clean ground after each calving. It is obvious that more study in the field in problem herds is needed to determine the sanitation needs and management practices to control this metritis syndrome in a practical way. Possibly by proper

construction, suitable isolation, adequate disinfection and rest after each calving, stalls could be constructed as have farrowing houses, that are adequate for the needs of intensive dairy farming.

Preventive treatment of cows in a herd where postparturient metritis develops in nearly every cow is generally not satisfactory. Autogenous bacterins or commercial polyvalent vaccines have been tried without success. Injections of oxytocin after calving seem to have little or no effect. Parenteral injections or local intrauterine infusions or capsules of broad range antibiotics after calving have limited value and then only in possibly preventing some cases of septic metritis. In one experiment where two 500 mg. of neomycin sulfate boluses were inserted into the uterus of cows within 24 hours of calving the number of services per conception were greater in the treated than in the control cows.²⁶ As an aid to hastening the recovery of the chronic metritis and delayed involution of the uterus, estrogen injections or 3 to 10 mg. of estradiol and intrauterine antibiotics and/or weak Lugol's solution, 2 to 5 ml. of Lugol's solution in 100 ml. of water, infused into the uterus at biweekly or monthly intervals has proven helpful. Although proper management, exercise, and clean, noninfected isolation facilities for the parturient cow are more difficult for the farmer to provide, at present it is the best way to control this economically costly metritis syndrome.

Puerperal Laminitis is most likely to occur in the mare and may be commonly seen in the cow, ewe, and sow. Twenty-four percent of 170 cases of bovine laminitis occurred within 2 to 3 days of calving.^{50a} It usually occurs secondary to a septic metritis. In the mare the placenta may tear away, leaving the apex of the allantois chorion in the nongravid horn. This placental remnant acts as a focus of infection and the uterus fills with a fetid, watery exudate. Laminitis is apparently caused by the septic uterine contents and possibly the histamines released and results in symptoms similar to those in laminitis of digestive origin. Usually 2 to 4 days after parturition the animal begins to exhibit a foundered gait characterized by the hind legs being placed well forward under the body in order to remove the weight from the even more severely affected forelimbs. The hooves are hot to the touch and the digital artery has a strong, hard pulse. The animal may lie down continually, standing for only short intervals, or rarely it may refuse to lie down. Weight loss is rapid. The prognosis is fair if treatment is begun early. Any animal with hooves with severe retained placenta or septic uterine infection should be treated early to prevent the possibility of laminitis developing. Treatment consists of the administration of an antihistamine in repeated doses plus the application of

ice packs to the feet or having the animal stand in cold water. The author prefers alternate hot and cold packs and placing the animal on a firm supportive bedding such as sand. The placenta of any valuable mare should be examined after expulsion by the veterinarian or, if he is intelligent and informed, by the owner to make certain that none of the placenta has remained in the uterus. If laminitis develops in a mare or other animal several days post partum, the uterus should be treated as for septic metritis by gently removing the exudate and placenta if present. Antibiotics may be used in the uterus and parenterally along with injections of oxytocin. The uterus should be examined and treated again if necessary in 24 to 48 hours and therapy continued until recovery results. Phenylbutazone or similar nonsteroid antiinflammatory drugs and possibly tranquilizers make the affected mare more comfortable and speed recovery by allowing moderate exercise to promote circulation in the hooves.

Puerperal Tetanus may occasionally occur in the mare and cow. It is possible in any species. All mares with dystocia, retained placenta and metritis and prolapsed uteri should be vaccinated promptly with tetanus antitoxin or toxoid. In the cow, even though of unusual occurrence, puerperal tetanus is the most common form of the disease. It often follows retained placenta and postpartum metritis. Unsanitary handling of a retained placenta when the uterus or birth canal may be traumatized predisposes to tetanus in the cow and mare. The afterbirth drops out a short distance when the cow lies down and becomes contaminated and when the cow rises foreign material on the placenta is drawn into the genital tract. Tetanus is usually observed one to four weeks after parturition. In many cases a post-*puerperal* metritis is present. If possible the uterine exudate should be removed and the cow or mare treated as for an ordinary case of tetanus resulting from external wounds, that is, by the administration of large doses of tetanus antitoxin, penicillin and tranquilizers. Estrogens or prostaglandins, if a corpus luteum is present, should be injected to evacuate the pus from the uterus. Constant, careful, quiet nursing is essential. The prognosis is guarded but recovery may occur if the cow is treated early with an indwelling uterine catheter to infuse the uterus with about 50 to 100 ml of penicillin-streptomycin mixture daily and inject 5,000 units of tetanus antitoxin followed by 1500 units daily for a number of days. A tranquilizer and laxative may also administered as needed.³⁶

Uterine Abscess, or pyometra with cervical or vaginal obstruction, may occasionally follow severe septic metritis, dystocia, and necrotic cervicitis or vaginitis that cause an atresia of the birth canal. It is seen in all species, but most commonly in the cow and mare. During the early stages no external symptoms may be evident

but after several weeks to a month or more the uterus becomes so greatly distended with pus that it may cause a distention of the abdomen. Usually intermittent straining and frequent urination are present. On rectal and vaginal examination the enlarged fluctuating uterus can be felt protruding into the pelvic cavity and the stenotic or closed portion of the genital canal may be palpated. Adhesions between the vagina and uterus may be present, so that an incision can be safely made through the vaginal wall into the uterus to drain off the pus. In one mare so treated by the author about 15 gallons of pus were removed. Symptoms of shock developed following the removal of this large volume of pus. The uterine abscess may break into the rectum or vagina. The animals occasionally recover, but their breeding life is ended. This condition should be distinguished from an abscess of the uterine wall which is a small, localized lesion.

Infections of the Cervix, Vagina and Vulva

Postpuerperal Cervicitis due to trauma, mild lacerations, infectious material from the uterus passing through the cervix, infection by extension from the vagina, or infection from a retained placenta or material carried into the genital tract on the placenta, is common in animals. It is observed most commonly in the cow and in association with a metritis or vaginitis after calving. The good blood supply, large mucus glands in the cervix, and the folded mucous membrane make severe injury, necrosis, and atresia of the cervix rare except in the mare. If cervicitis is present in the mare the gentle introduction of mild oily antiseptics or antibiotic infusions into the uterus and gentle dilation of the cervix with the gloved fingers may prevent stenosis occurring. This should be repeated until the cervicitis has been corrected. As long as a metritis is present local treatment of the cervix is usually ineffective. Once involution of the uterus takes place and the uterus rids itself of infection, the cervix also recovers unless a vaginitis, pneumovagina, or a greatly enlarged chronically infected ectropic cervix persists. Treatment for postpuerperal cervicitis is the same as treatment for metritis or vaginitis. The prognosis is usually good.

Postpuerperal Vaginitis and Vulvitis may occur with or without a concurrent metritis. Following parturition either a severe necrotic vaginitis and vulvitis or a mild catarrhal inflammation of these structures may develop.

Necrotic Vaginitis, Vestibulitis and Vulvitis is observed most often in dairy and beef heifers having a narrow small birth canal that caused dystocia. The fetus may have been expelled without aid after a difficult, prolonged parturition or traction may have been necessary. These factors, especially the latter, result in trauma, lac-

eration, excessive pressure, and abrasion of the vulvar and vaginal walls. The mucosa of the vagina and vulva may be further irritated by the presence of a retained placenta, a metritis, or a torn or ruptured perineum allowing infection to enter the vulva and vagina. Pressure necrosis of the vulvar and vaginal mucous membranes is often observed following the removal of an emphysematous fetus by traction or after a prolonged fetotomy without proper lubrication in a heifer or cow. In rare cases necrotic vaginitis may be due to douching with too irritating or strong an antiseptic. Occasionally a severe necrophorus infection of the vagina may occur.

The symptoms of necrotic vaginitis and vestibulitis are usually observed 1 to 4 days after parturition and last for 1 to 2 weeks or more depending on the severity of the lesions. There is usually an arched back, elevated tail, anorexia, and rapid loss of weight. The animal may exhibit either no straining, straining that is intermittent and mild and only observed at the time of urination or defecation, or nearly continuous straining with air being sucked into the vagina and forcibly expelled. The vulva, vestibule and vagina may be very swollen, due to a perivulvar and perivaginal phlegmon. A fetid, reddish, watery fluid is present. The pulse rate is usually elevated. The body temperature may be moderately elevated. Parting of the vulvar lips reveals a necrotic, diptheritic inflammation of the vestibule and vagina, usually most severe at the vulvo-vaginal border. The necrotic portion of the mucous membranes sloughs, and the exposed submucosal tissues granulate and eventually heal with a cicatrix. In an acute case, the passage of the hand through the inflamed vulva and vagina of the cow is likely to cause bleeding. This act is very painful to the animal and because of the swollen dry tissues is usually difficult to perform. Straining is probably due to the vestibular and vulvar inflammation and irritation and possibly the accompanying vaginal swelling or phlegmon, since there are many sensory nerves in the vulva and vestibule but few if any in the vagina. Straining due to vulvitis, vestibulitis and vaginitis should be differentiated from that caused by dystocia, an undiagnosed, retained fetus, rabies, or other conditions which might cause straining.

In some of these cases of vulvitis, vestibulitis and vaginitis, no matter how they are handled, marked stenosis or even atresia of the vagina may occur resulting in a distention of the cranial portion of the vagina due to pus or mucus. In advanced chronic cases, even the cervix and the uterus may be distended with 2 to 3 gallons of a mucopurulent material if infection persists, or of mucus alone if no infection is present. The prognosis is fair to good in mild cases treated early. In severe cases that are neglected the prognosis is guarded. If necrosis is extensive, straining constant, and the animal is extremely

debilitated, death may result. In cases of severe vaginal or vestibular atresia—fortunately uncommon—the future breeding life is usually terminated.

The treatment of necrotic vaginitis should be gentle and conservative. Oily bland antiseptics such as 4 to 6 ounces of bismuth formic iodide or antibiotics, in oil, together with the broad range antibiotics, may be introduced in a gentle manner into the cranial portion of the vagina 2 to 3 times a day. As this infusion is expelled it coats the inflamed mucous membranes. If swelling, phlegmon, elevation of the temperature, and rapid pulse rate are present, parenteral administration of antibiotics and/or oral or intravenous administration of sulfonamides are indicated daily for 4 to 6 days or until recovery is evident. If in the cow, retained fetal membranes are hanging through the vulva they should be removed if this can be done easily and without injury to the vulva and vagina. In most cases the placenta is fastened securely and must be allowed to remain and drop away later. If the membranes are heavy and hang nearly to the floor they should be cut off at the hocks so the added weight does not aggravate the vulvitis and induce straining. If straining is present, the use of one of the longer-lasting epidural anesthetics such as lidocaine to which a small amount of adrenaline solution has been added to retard its rate of absorption. This may be given twice daily or more often if necessary. Sometimes procaine penicillin may be used epidurally as a fairly long-acting local anesthetic. The administration of tranquilizers is helpful in controlling pain and tenesmus. Elevation of the rear parts may be helpful. In mild cases of vulvitis and vaginitis with straining, some local anesthetic ointments containing butesin picrate or benzocaine have been used but difficulty has occurred in applying these to a moist mucous membrane and their effect is questionable.

If tenesmus is severe and accompanied by marked sucking and blowing of air into and out of the vagina, the dorsal two-thirds to three-quarters of the vulva should be tightly sutured after administration of epidural anesthesia. This prevents ballooning of the vagina with air and precludes the accompanying irritation and straining. This treatment with other supportive treatments described usually promptly controls the straining. The sutures holding the vulvar lips together may be removed in 4 to 7 days. In rare cases it may be indicated to insufflate the abdominal cavity with air to prevent tenesmus.⁶³ Control of severe straining is essential to prevent rapid loss of weight, weakness, early exhaustion, and even death. Repeated treating and dilating of a necrotic vagina is not indicated, inasmuch as this procedure prolongs recovery time, increases the inflammatory reaction in the vagina, and produces additional scar tissue. Fol-

lowing healing, breeding may be advised if the stenosis is not severe. At the time of parturition it may be necessary to dilate the stenotic portion of the vagina. In many cases, however, due to the relaxation of the vaginal wall and surrounding tissues, mild stenoses disappear at the time of parturition. If the stenosis is severe and breeding is desired this might be accomplished by artificial insemination with cesarean section at the time of parturition. Most severe cases of stenosis of the vagina are slaughtered. Outbreaks of blackleg have been reported in sheep following lambing where the organism, *C. festeri*, invades the damaged vulvar tissues.¹¹

Catarrhal Vaginitis and Vulvitis occurs following or with retained placenta, puerperal metritis, or injuries to the vulva causing pneumovagina. Following parturition this generally is characterized by a persistent mucopurulent discharge from the vulva. The prognosis is good. Dilute, warm vaginal douches, using 200 ppm Betadine solution, dilute Lysol or other soapy aromatic antiseptics, or saline or sodium bicarbonate, are indicated. These may be repeated at 1- to 3-day intervals. If the vulva is torn it should be sutured, to prevent pneumovagina. If puerperal metritis is present the vaginitis may persist in a mild form until the discharge of uterine exudate ceases. In some cases when only a vaginitis is present one to three weeks after parturition, some oily antibiotics or antibiotics in ointment form may be placed in the vagina to aid in overcoming the infection.

Puerperal and Postpartum Infections of the Genital Tract

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Paraplegia in the Parturient Cow, The "Downer Cow" and "Fat Cow Syndrome" ("Atypical Milk Fever," "Creeper" or "Alert Downer")

The cow that fails to rise after calving or dystocia, the cow that goes down and is unable to rise late in gestation

or soon after parturition or the cow that goes down with parturient hypocalcemia and fails to respond to treatment cause a perplexing diagnostic problem for the veterinarian. All too often many of the following conditions are lumped together without adequate and careful attempts to make an accurate diagnosis and called a "downer cow," a "creeper," an "alert downer" or a cow with "atypical milk fever." Most of these cases reflect the disease state present in the cow entering the periparturient period and the stresses and injuries developing during this period. Each case should be studied carefully. A complete physical examination of each system of the animal should be performed despite the fact the animal is recumbent. Since diseased states occurring around calving may be serious an early diagnosis, treatment, and recovery is desirable from the standpoint of the animal's future production of milk and/or calves.

Overconditioned dry cows, often fed excessive amounts of corn silage high in energy, have an increased susceptibility to metabolic and infectious diseases including milk fever, ketosis, displaced abomasum, retained fetal membranes, secondary metritis, mastitis, and foot and joint diseases that are loosely described under the "fat cow syndrome." If these animals are unable to rise for a period of a few hours pressure damage to muscles and nerves may occur. In some herds with this nutritional problem brought on by poor management the morbidity rate may reach 50 to 90 percent and the mortality rate may reach 20 percent or more.^{7,9}

The "downer cow" syndrome can be regarded as a common complication of parturient hypocalcemia that is preventable to a significant extent by either preventing milk fever or giving early treatment when the standing cow initially shows inappetence, mild depression and cold extremities.⁹ In a recent study 16 normal healthy cows confined by halothane anesthesia in sternal recumbency on the right side for 6 to 12 hours developed pressure damage including ischemic necrosis of muscles and sciatic and peroneal nerve lesions. Eight of the 16 cows were able to rise within 3 hours after anesthesia but the other 8 cows remained recumbent until death or euthanasia.^{4a,b}

A check-list of factors and possibilities to consider in the diagnosis of paraplegia before, at and after parturition includes:¹¹

A—Metabolic and/or Nutritional Disturbances

1. Parturient paresis, hypocalcemia, milk fever.
2. Tetany, hypocalcemia and/or hypomagnesemia including grass and transport tetany.
3. Ketosis, usually postparturient.
4. Debility, cachexia, or weakness—due to starvation, senility, acute or chronic wasting dis-

eases including internal or external parasitisms and Johne's Disease.

5. Zenker's degeneration of muscle—due to a lack of selenium, vitamin E, and the presence of other factors including poor quality hay and muscle stress following a lack of exercise or following vigorous attempts to rise in cows with milk fever, nerve paralyses, or cows that are cast.

B—Traumatic and/or Physical Injuries—These often occur during attempts to rise especially where the footing is slippery or in cows affected with parturient hypocalcemia resulting in pressure damage to muscles and nerves.^{4a,b}

1. Paralyses—due to injuries to the obturator, L6-sciatic, peroneal, gluteal, femoral, and brachial nerves or compression of spinal cord. Besides a severe injury, lymphosarcoma and abscesses may also produce spinal cord compression.^{12,14}
2. Dislocation of the hip or sacroiliac joints,^{1,10} (See Figure 101). The latter is seen in young cows, under 5 years of age, often after a dystocia.
3. Fractures of the leg, pelvis, spine, and skull.
4. "Cast" often associated with myositis, Zenker's degeneration, tendinitis, arthritis, muscle asthenia and ischemia, phlebitis and thrombosis, and contusions.
5. Rupture of the gastrocnemius muscle, usually secondary to Zenker's degeneration.
6. Exhaustion from attempts to rise or exertion from dystocia may produce a circulatory crisis, low blood pressure and myocarditis.¹³ This may be related to a lack of exercise.
7. Hemorrhage, anemia, or shock as in rupture of the uterine or pelvic blood vessels in torsion or prolapse of the uterus, laceration of the genital tract, transportation in advanced pregnancy, violence during foaling in mares, abomasal or duodenal ulcers, coccidiosis, anaplasmosis, leptospirosis and postparturient hemoglobinuria.

C—Infectious Diseases or Inflammatory Processes

1. Septic metritis, with or without a retained placenta or a vulvar discharge.
2. Septic mastitis.
3. Peritonitis, or pericarditis, secondary to traumatic gastritis, uterine rupture or abomasal ulcers with perforation.
4. Acute laminitis.

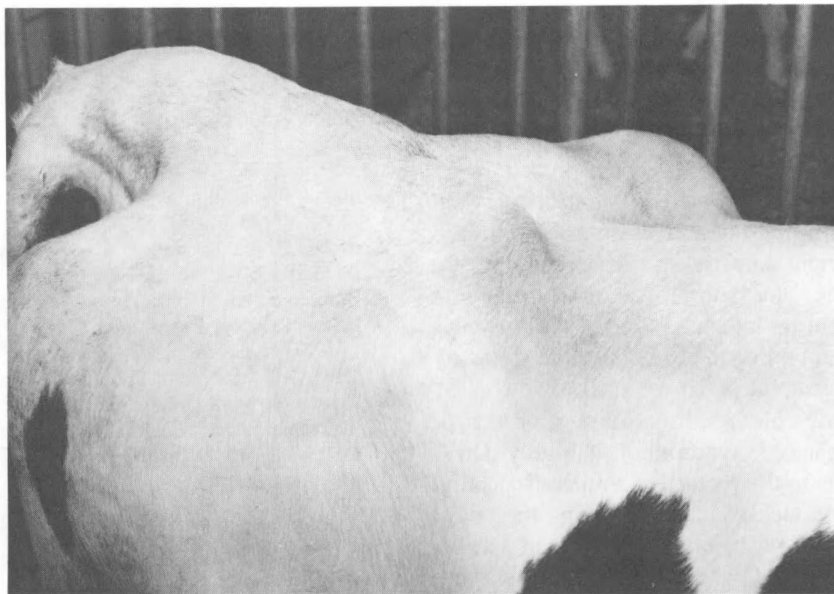


Figure 101. Dislocation of the sacroiliac articulation in a cow. This is occasionally seen in young dairy cattle following a difficult parturition.

5. Septic arthritis—knee, hocks, coffin joint.
6. Miscellaneous diseases—severe pyelonephritis, shipping fever, blackleg, anthrax, necrobacillosis, rabies, listeriosis, meningitis, and brain or cord abscess.

D—Digestive Disturbances, Diarrheas, Toxemias and Poisonings

1. Enteritis, severe diarrhea secondary to an intestinal stasis associated with hypocalcemia or grass tetany, winter dysentery, salmonellosis, virus diarrhea, etc.
2. Toxic indigestion due to overeating on fruit, grain, or spoiled forage.
3. Toxic indigestion of advanced pregnancy has been described⁵ as occurring in stabled dairy cows late in the winter confinement period and characterized by partial to complete anorexia, dullness, progressive emaciation and increased pulse rate. Normal activity of the gastrointestinal tract appears impaired possibly due to large gravid uterus. The recommended treatment consists of exercise, forced if necessary, intravenous fluid therapy, and mild laxatives orally. In a valuable cow cesarean section or induced parturition might be indicated.
4. Poisonings—plant, chemical, etc.

E—Miscellaneous Causes.

1. Hydrops allantois and/or amnii.
2. Lymphocytoma especially involving the spinal cord, heart, and abomasum.
3. "Maligner."
 4. Spastic syndrome ("stretches").
 5. Severe albuminuria and uremia secondary to nephritis (rare).

In making a differential diagnosis of the etiology for paraplegia, cows with infectious diseases may have an elevated body temperature and pulse rate. The latter is also elevated in digestive disturbances. Hypocalcemic states usually respond to calcium therapy intravenously or udder inflation although some response to calcium therapy may be observed in digestive disturbances. An expiratory grunt is often exhibited in cases of peritonitis. One or more of the following symptoms would be sufficient reason for questioning the diagnosis of parturient hypocalcemia in a cow: a pulse rate of 90 or more per minute, rapid respirations or respirations accompanied by an expiratory grunt, diarrhea, an attitude that is bright and alert, a nearly normal appetite, a body temperature of 102° F. or higher, a hot swollen udder, persistent tenesmus, and failure of expected response to adequate calcium therapy. Although these diseases and conditions are described and listed for cows many of them are applicable to mares, ewes, sows, and even bitches and queens.

Because of his exposure to frequent necropsies on so-

called "downer" cows the author is impressed with the frequency of physical and muscular lesions in these cases as well as the variety of the conditions found. A high incidence of muscle damage and tears together with a rising S.G.O.T. level in "downer" cows following parturient paresis was observed.^{3,4} The best procedure to follow to prevent "downer" cows is to control, prevent or provide early and prompt treatment of cows with hypocalcemia or parturient paresis.⁸ In certain herds in selenium deficient areas, the administration of selenium late in gestation might be indicated to assist in preventing Zenker's degeneration of muscle under the stress of calving or during parturient paresis.

The author is firmly convinced that obesity or excessive condition "the fat cow syndrome," is highly detrimental and dangerous to the parturient animal especially if it is coupled with a lack of exercise during the latter half of the gestation period. In cases of parturient paresis these two factors combine to greatly lower the cow's resistance to stress, to favor exhaustion and a "malinger-type" of attitude and to result in difficulty in rising with the production of secondary traumatic lesions. A 20 by 20 box stall with a dirt floor for excellent footing is highly desirable for large high-producing parturient dairy cows to avoid injury. Further proof of the possible effect of lack of exercise is the list of diseases of muscular organs that are most commonly observed in cattle in northeastern U.S. in the late winter or early spring months after a long period of confinement namely: displaced abomasum or torsion of the abomasum, prolapse of the vagina, prolapse of the uterus, retained placenta possibly related to uterine inertia, torsion of the cecum, intussusception of the intestine, torsion of the uterus, indigestion of advanced pregnancy and Zenker's degeneration of skeletal muscle. The incidence of these diseases is much lower

during the late spring or summer months when cows are on pasture and getting exercise.

Paraplegia in the Parturient Cow

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Part II

INFERTILITY IN DOMESTIC ANIMALS

Although the problem of infertility in domestic animals has been studied for many years there has been a great surge of interest, activity, research, and investigation since 1940 when the widespread use of artificial insemination forcefully brought the problem of infertility in domestic animals, to the attention of farmers, veterinarians, animal husbandrymen, physiologists, endocrinologists and others. These basic studies on the problem have rapidly forwarded our knowledge of reproductive physiology in domestic animals. In the past 25 years basic and applied reproductive studies in all species of animals and man has been heavily supported by state and federal governments, as well as private foundations, because of the urgency of thoroughly understanding all areas of reproductive physiology so that effective methods may be devised to control the so-called population explosion. In that time there has also been rapid progress in the field of endocrinology. Nutritional studies have furthered our knowledge of infertility as related to the animal diet.

The losses due to sterility and delayed breeding in dairy cattle were estimated in 1960 to be about twenty million dollars per year in New York State.² While it is possible that the incidence of sterility and delayed breeding is increasing, it is more likely that in recent years, due to more general use of artificial insemination, gradually,

increased milk yield, higher value per cow, and increasing nutritional problems, farmers have become more conscious of their loss than they were formerly when a cow failed to conceive promptly. The average good cow should provide a farmer a net return of \$500 each year over feed costs. Each monthly delay in conception results in \$30 to \$60 loss to the farmer. Preventive medicine is a component part of the control of infertility and as such requires an adequate record keeping system not only for informational purposes but also for evaluation of performance and identification of deficiencies.

The studies initiated in the field of artificial insemination on the infertility problems in bulls and cows have done much in recent years to elucidate more clearly the importance of the bull in the overall problem of bovine infertility. These studies in cattle have in turn set the pattern and stimulated studies in the other species of animals.

In the past 20 years reproductive studies in horses, swine, dogs and cats have grown and expanded rapidly. The increased value of the large domestic animals and the realization by the owners that knowledge is available to greatly improve reproductive rates and reduce economic losses has increased the demand for skilled veterinary services.

Chapter XII

PHYSIOLOGY OF FEMALE REPRODUCTION

Reproductive Hormones

Reproduction is a luxury function of the body not physiologically necessary for the life of the individual and usually not performed until the animal reaches nearly adult size and nutritive supplies are ample for the nutrition of both the dam and fetus. Any adverse influence of environment, nutrition, stress or disease on the individual will, if severe enough, exert its influence on the reproductive system.

Reproduction in mammals is largely controlled by endocrine glands and the hormones they secrete. These influence all phases of reproduction. At least four temporary reproductive structures or organs elaborate various steroid or protein hormones; these are the ovarian follicle, the corpus luteum, the placenta and the endometrial cups in the mare. The hormonal regulation of reproduction is a complicated and carefully balanced system of checks and controls. The various hormones stimulate or inhibit each other and accordingly their effects on the animal's reproductive organs. The reproductive hormones play a major role in the initiation and regulation of the estrous cycle, ovulation, fertilization, preparing the uterus for the fertilized ovum, protecting, insuring and maintaining pregnancy, initiating parturition, and the development of the mammary gland and lactation. With a complex hormonal system controlling these many phases of reproduction, it is remarkable how seldom reproductive troubles are due to a breakdown of any portion of this mechanism. The nervous system, both central and autonomic, plays a secondary role in reproduction but one that is closely linked to the hormones produced. These nervous mechanisms in reproduction play a definite role in ovulation in those species in which ovulation is not spontaneous; with the period of sexual desire, or estrus and acceptance of the male and in such hormonal disturbances as nymphomania. Thus reproduction is under neuroendocrine or neurohumoral control. In many species of animals all phases of reproduction can take place even with the spinal cord severed in the lumbar region.

The reproductive hormones of each mammal are not species-specific in their effect; that is, the estrogenic hormone from women or mares when injected into a cow

produces the same effect as does the estrogenic hormone from the cow. All hormones are highly specific and selective in their action on the genetically-conditioned end, or "target," organ. The "target" organ with its receptors reacts promptly to a specific hormone to produce the substance or changes for which it has been genetically "programmed." Differences in the amounts of hormone required to produce specific effects occur between species, but the basic effects thus produced are often similar. A wide range of reactions to certain hormones exists.

Another important fact to recognize in the use of reproductive hormones is that hormones produced in a certain organ or gland do not, when injected, affect that organ or gland directly. In other words, endocrine disturbances of the ovary do not respond directly to the ovarian hormones, but if curable usually respond to the pituitary or uterine hormones. For example ovarian hormones act in a direct manner on the tubular genitalia and in an inhibitory manner on the anterior pituitary gland through their indirect effect on the central nervous system and hypothalamus. The amount of hormone, the frequency of dosage, and the time of injection in relation to the stage of the estrous cycle have profound influences on the effects produced.

Many external sensory stimuli act upon the central nervous system and hypothalamus and effect reproduction. These include: light, and sight mediated by the eyes, sound, or vocalization, mediated by the ears, smell mediated by the nose, state of nutrition, physical stimuli including cold and heat and the amount of work, stress as mediated by the release of glucocorticoids from the adrenal gland, tactile stimuli as obtained by mounting and intromission and possibly others. The olfactory stimuli have been called "pheromones."¹⁰ Certain drugs, as well as hormones, can effect the centers in the central nervous system and produce changes in reproductive physiology. In the central nervous system, spinal cord and hypothalamus are numerous interacting reflex arcs, and centers concerned with reproductive behavior and with production of releasing factors, peptides or neurosecretions that result in the release of the tropic hormones from the anterior pituitary gland after they pass to the

adenohypophysis through the hypophyseal portal system. Such centers, often located in or near the hypothalamus, also control the release of prolactin from the anterior pituitary gland and oxytocin and vasopressin from the neurohypophysis or posterior pituitary gland (see Figure 102). The blood supply to the hypophysis and hypophyseal portal system used to carry releasing factors or neuroendocrines from the hypothalamus to the adenohypophysis has been described.⁵

In the last 20 years much work has been done to elucidate the relationship of the hypothalamus and its releasing factors to the central nervous system and the adenohypophysis.^{3,6,8} These releasing factors (RF) are small peptides that like the other hormones are not generally species specific. The hypothalamic releasing factor or hormone in ACTH is CRH, corticotropin releasing factor; for TSH is TRH, for FSH and LH is GnRH, and for STH or GH is GRH. In regard to prolactin a hypothalamic factor inhibiting its release from the adenohypophysis, PIF or PRIF has been described. GnRH, gonadotropin releasing hormone, is a decapeptide that has been synthesized and produced commercially as "**Cystorelin**." GnRH is sometimes referred to as LHRH or LHRH/FSHRH because the single hormone acts on the adenohypophysis to release both luteinizing hormone (LH) and follicle stimulating hormone (FSH).⁶ Both GnRH ("Cystorelin") and human chorionic gonadotropin (HCG) are equally effective in the treatment of cystic ovaries in cows.^{3,6,8}

The principal or major endocrine gland controlling the reproductive organs and functions is the adenohypophysis. The pituitary gland is composed of two principal parts. The anterior lobe or adenohypophysis is quite vascular. Cells in this lobe produce the gonadotropic hormones and control the activity of the gonads. The posterior lobe or neurohypophysis is divided into the pars nervosa and pars intermedia. The latter structure is small and apparently of limited importance. The pars nervosa, the major portion of the posterior lobe, is attached to the floor of the third ventricle or hypothalamus by a stalk or infundibulum. Thus the anterior and posterior lobes of the pituitary gland are separate and distinct in origin, structure and functions. (See Figure 102.)

Anterior Pituitary or Adenohypophyseal Hormones

There are 6 major adenohypophyseal hormones that have been isolated and are obtainable in a nearly pure form at the present time:

ACTH—adrenocorticotrophic hormone.

Prolactin—this hormone promotes lactation and certain other metabolic and possibly gonadotropic functions.⁶

STH or GH—somatotrophic or growth hormone.

TSH or TTH—thyroid-stimulating or thyrotrophic hormone

FSH—follicle-stimulating hormone

LH—luteinizing and luteotropic hormone

MSH—melanocyte—stimulating hormone—this seventh hormone is of little importance
(FSH and LH are the gonadotropic hormones.)

All of these hormones are complex proteins in nature and are water-soluble. A review of the literature on the histology and physiology of the anterior pituitary gland reported that there were three principal cell types composing this endocrine gland; basophilic cells, acidophilic cells and chromophobe cells. FSH, LH, TSH, and probably ACTH are produced by certain basophilic cells. Somatotrophic or growth hormone and prolactin are produced in the acidophilic cells.^{3,6,8}

The adrenocorticotrophic hormone is essential for the maintenance and functioning of the adrenal cortex. It is sometimes called the "stress" hormone because it stimulates the production of glucocorticoids from the adrenal cortex. Besides its other functions, this latter hormone raises the blood sugar level and lowers milk production. This explains the value of ACTH and the glucocorticoid hormones in acetoneuria or ketosis. The adrenal cortex is capable of synthesizing the gonadal steroid hormones as well as the glucocorticoids. The effects of stress on the reproductive system have been reviewed.⁴¹ **The thyrotrophic hormone** is essential for the functioning of the thyroid gland and the regulation of metabolism by its stimulation of thyroxine production. **The somatotrophic or growth hormone** is concerned with body growth; moreover, it has been shown to be intimately concerned with udder development and lactation. Somatotropin causes growth of the long bones, affects protein metabolism by increasing nitrogen retention by the body, and markedly influences carbohydrate metabolism. This hormone in the cow is probably more concerned with lactation than is prolactin. Recent studies have shown that natural or recombinantly-derived bovine growth hormone when injected into cows the third month of lactation in daily doses of 25 mg increased milk production 10 to 13 percent and improved feed efficiency 9 to 15 percent.^{2a,c}

The two anterior pituitary hormones concerned with reproduction are FSH and LH, the gonadotropic hormones. Probably prolactin should not be listed as a gonadotropic hormone in domestic animals.⁸ **FSH or fol-**

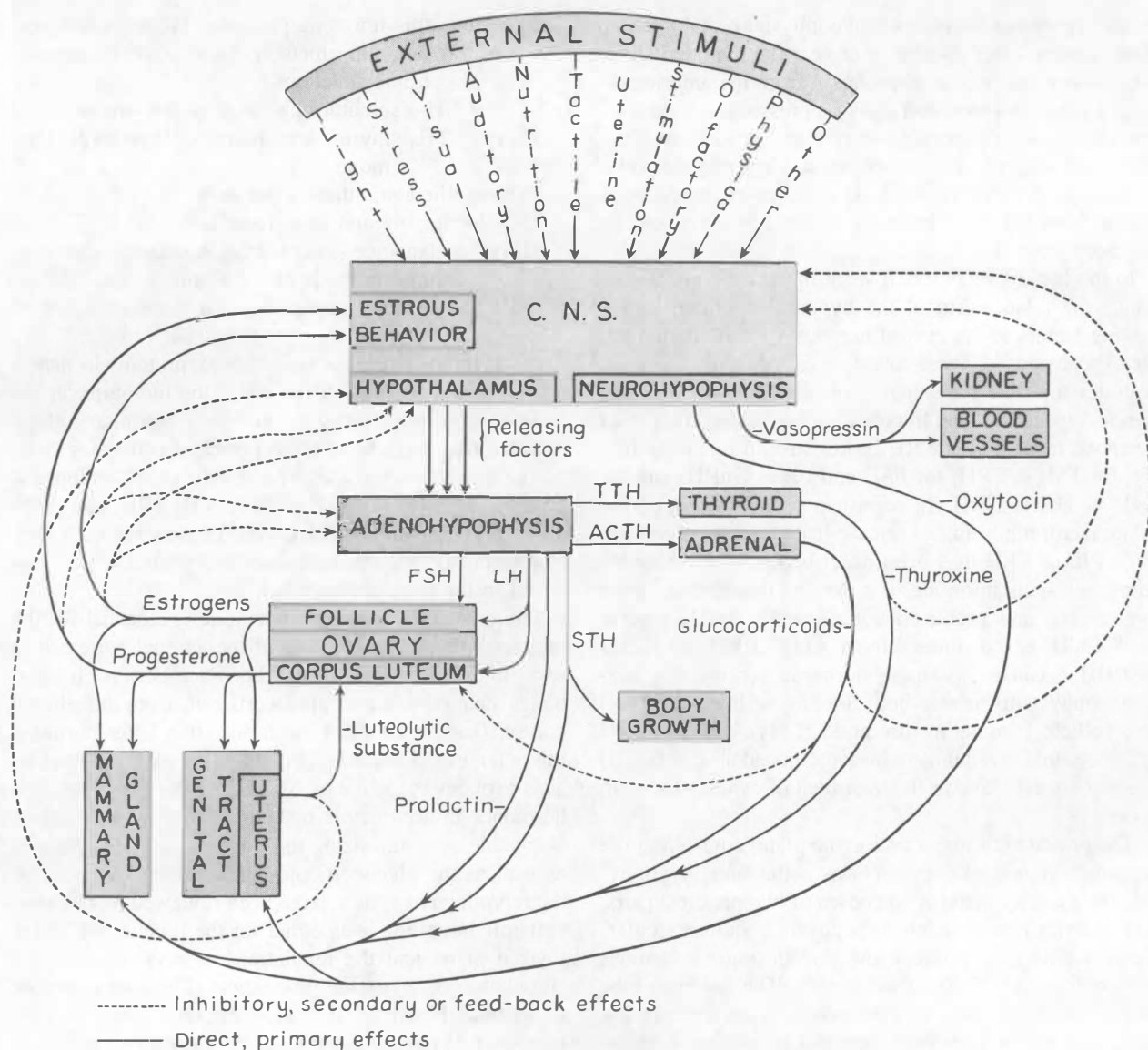


Figure 102. Diagram of the Neuroendocrine Control of Reproduction in Female Animals.

Luteal-stimulating hormone is necessary for the growth of the Graafian follicles and the production of estrogens in the ovary. The secretion of this hormone was formerly thought to be inhibited only by progesterone from the corpus luteum, by testosterone from the interstitial cells of the testes, or by estrogen from the follicular cells and fluid. This was considered to be a "feedback" effect of the steroids on the central nervous system and hypothalamus preventing the secretion of GnRH. For this reason in castrated animals or postmenopausal women, the plasma levels of circulating FSH and LH are high. Recent studies have indicated that a nonsteroidal substance

in the follicular fluid has an inhibitory effect on FSH secretions and plasma levels in mares and ewes.^{28c} Luteinizing hormone (LH) is released in a pulsatile or episodic pattern or fluctuations.⁶ **LH, luteinizing or luteotropic hormone** causes ovulation and growth of the corpus luteum from the granulosa cells of the ruptured Graafian follicle. The basophilic delta cells of the anterior pituitary gland produce LH and probably FSH.^{3,6,8} The continued secretion of LH is necessary to maintain the corpus luteum and the secretion of progesterone to continue pregnancy in the cow. LH is probably luteotropic for all domestic animals.⁸ Prolactin is also luteo-

tropic. LH and probably FSH secretion and release can be stimulated by the drug, clomiphene.¹³ The following drugs can inhibit or prevent LH release and ovulation: antiadrenergic agents like dibenamine; anticholinergic agents like atropine; tranquilizers like chlorpromazine; psychic energizers like iproniazid; anticonvulsants, sedatives and anesthetics like barbiturates; and analgesics like morphine. These drugs act in a variety of ways on the cells of the C.N.S. to prevent or inhibit the release of LH. FSH and LH are synergistic in their action on the gonads. **Prolactin** is primarily involved in the initiation and possibly the maintenance of lactation. It is believed to be intimately connected with maternal instincts in mammals and broodiness in hens. It may be luteotropic in ewes.^{8,37}

Because of the many essential hormones produced by the anterior pituitary gland, it has been often called the "master gland" or "motor" of the endocrine system. In the light of recent studies this designation is questionable as it is obvious that the pituitary gland is controlled by the higher reproductive "centers" in the central nervous system. Clinical abnormalities of this gland produce many and varied effects. Since the hormones produced by this gland are complex proteins, they cannot be produced synthetically and have no effect when taken orally inasmuch as they are destroyed by the proteolytic enzymes in the digestive tract. DuVigneaud, however, won the Nobel Prize in chemistry in 1954 by synthesizing the neurohypophyseal hormones, oxytocin and vasopressin which are complex polypeptides made up of 8 amino acids. Other workers are busy studying the structure of other pituitary hormones and it is likely more may be synthesized. Repeated injections of heterologous anterior pituitary hormone products into animals may result in the production of antihormones, with the result that the injected hormone is neutralized or no longer effective. This is probably of little importance in most animals and seldom occurs unless repeated injections of these proteinaceous hormones obtained from animal sources are administered.^{7,32,42}

The adenohypophyseal content of LH is highest in cattle, sheep and cats and lowest in horses and man.⁸ Of the domestic animals, the cow and ewe secrete the greatest amount of prolactin. It has been shown that the timing of the release and the amounts of FSH and LH hormone released is very important in the initiation of ovulation and the number of ova released. The blood serum of castrates contains an increased amount of FSH because neither testosterone, estrogen, nor progesterone is inhibiting its secretion. Large prolonged injections of these latter steroid hormones suppress pituitary gonadotropic hormones and cause small, atrophic gonads. Smaller

doses of estrogens or progesterone may cause cystic ovaries. The urine and serum of pregnant women from about 30 to 60 days after the last menstruation and the serum of pregnant mares from about 40 to 120 days of gestation contain large amounts of gonadotropic hormone human chorionic gonadotropin (HCG) and pregnant mare serum gonadotropin (PMSG) or equine chorionic gonadotropin (ECG), respectively. In the mare this hormone is not excreted in the urine. In humans these gonadotropic hormones are produced in the chorion of the placenta and called chorionic gonadotropins; in the mare they are produced by the endometrial cups of the uterus, which originated from the chorionic cells, and are called equine gonadotropins.

The equine gonadotropic hormones from pituitary glands and pregnant mare serum are predominately follicle-stimulating in character although a small amount of LH is present.^{34a} Sheep and pig pituitary gonadotropic hormones are predominately luteinizing in character although some FSH is present. Chorionic gonadotropic hormone from the urine of pregnant women is almost entirely luteinizing in character.

The biologic sources of the gonadotropic hormones are: human chorionic gonadotropin, HCG, from the urine of pregnant women is sold under many trade names such as "Follutein" (Squibb), and is prepared and packaged in the dry state in a sealed glass vial. This is reconstituted with a saline solution before use. In liquid form it retains its potency for several weeks or months if kept at refrigerator temperature. In rare instances anaphylactic reactions are observed in animals into which this product is injected. These reactions are most common in animals previously treated with this form of gonadotropic hormone. Human menopausal gonadotropin HMG, from urine is also used as a source of gonadotropin high in FSH.^{4b} **Anterior pituitary gland** extracts or pituitary gonadotropic hormones, FSH and LH are prepared from the pituitary glands of sheep, horses and pigs. Some of the more common veterinary preparations are "Vetrophin" (Diamond), a sheep pituitary product; "P.L.H." (Armour); and equine pituitary gonadotropin products such as FSH (Armour). These are purified and prepared in sealed vials as a dry powder and reconstituted with a saline solution at the time of use. Anaphylaxis following the use of these products is unusual. **Equine gonadotropic hormone** or pregnant mare serum gonadotropin, PMSG or PMS or equine chorionic gonadotropin (ECG)^{34a} is serum that is collected approximately every 10 days, between 50 and 100 days of pregnancy in the mare. The concentration of hormone is about 50 R.U. per ml. Repeated doses of this may cause anaphylaxis, especially in the cow. In the mare, rare cases of Theiler's disease

or infectious hepatitis have been reported to occur from 50 to 70 days to as long as 120 days after the use of this crude equine serum product.

PMSG in the mare's blood is present at 37 to 42 days of gestation and reaches a peak concentration at 70 days.^{4b} Shetland ponies have a concentration of 335,000 I.U. per liter of serum between 55 and 76 days of gestation. This is about twice as high as larger horses that have serum concentrations of 50,000 to 100,000 I.U./liter. Mares with twin fetuses have double the serum levels, 240 I.U./ml. vs 100 I.U./ml. of mares carrying single fetuses. Mares carrying mule foals produce only one-eighth as much PMSG as mares carrying horse foals. The mucoid secretion in the endometrial cups of the mares may contain 5,000 to 210,000 I.U./gm. of PMSG. Peak concentrations of HCG in human urine occur at 50 to 70 days of gestation when 20,000 to 450,000 I.U. of HCG per 24 hours of urine is excreted. After this period about 10,000 I.U. HCG is excreted daily to near term.

When the gonadotropic activity of the pituitary glands of man, horse, sheep, pig and ox were compared by assay on rats' ovaries highly sensitive to FSH the comparable percentages were 100, 35, 3, 2, and 1, respectively. When assayed on rabbits' ovaries highly sensitive to LH the comparable percentages were 100, 42, 62, 65, and 42, respectively. In the sheep, pig and cow FSH in the pituitary gland was low but LH was high. In the horse FSH and LH was high and in man FSH and LH were very high.

The principal use of gonadotropic hormones in animals is the administration of LH or luteinizing hormone in the treatment of nymphomania or cystic ovaries in cows to produce active corpora lutea and restore a normal estrous cycle. Other uses include the injection of luteinizing hormone at the time of estrus to hasten ovulation, or about 4 days after ovulation to increase the size of the corpus luteum and the amount of progesterone secreted. Injection of large doses of FSH or PMSG 4 to 5 days prior to estrus causes superovulation in the cow and ewe. The use of FSH to promote estrus in anestrus animals may be of value under certain limited conditions. Generally the results of this therapy for the treatment of anestrus have been poor. The value of gonadotropic hormones to produce descent of testes in cryptorchid animals is questionable. FSH and PMSG may be of value in producing estrus in sheep during the anestrus period in the spring and summer months and hastening the onset of estrus in lactating sows.

Protein hormones from the pituitary gland are ineffective if given orally because they are digested and broken down in the gut. They are water-soluble and may be given intravenously where they produce a rapid ac-

tion. These hormones given subcutaneously or intramuscularly are absorbed more slowly and provide a more prolonged effect. Protein hormones must be protected from thermal decomposition as they are heat-labile.

Posterior Pituitary or Neurohypophyseal Hormones

There are two neuroendocrine hormones secreted in the posterior lobe of the pituitary. **Oxytocin** produces its effect by contracting the smooth muscles such as those in the uterus, around the alveoli and lactiferous ducts of the mammary gland, and in the bladder and gut. This fraction of the posterior pituitary lobe was formerly called "obstetrical pituitrin." **Vasopressin** or "surgical pituitrin" causes contraction of the smooth muscle of the arterioles thus checking postpartum uterine hemorrhage and raising blood pressure. This is also an antidiuretic hormone, ADH. If ADH is deficient in the dog and cat,⁸ diabetes insipidus with symptoms of polyuria and thirst occurs. In this disease vasopressin is not present to regulate the water resorption from the glomerular filtrate in the kidneys.

Oxytocin and vasopressin or ADH are very similar in composition with 6 of the 8 amino acids in these two hormones being similar. Posterior pituitary hormone or extract is a stable extract of the posterior pituitary lobe containing both fractions, oxytocin and vasopressin. A combination of both fractions, rather than one alone, seems to give as good or better results than oxytocin alone for most conditions treated in the veterinary field. However, since oxytocin is produced synthetically, it is the one now generally available commercially for use in animals. These hormones are protein in nature and water-soluble. They are stable and are usually packaged in liquid form with a concentration of 10 or 20 U.S.P. (I.U.) units of each fraction per ml of the solution. Evidence of anaphylaxis following injection of oxytocin or vasopressin is rare in animals but it was seen occasionally when the former crude hormone extract was injected intravenously in the mare.

The posterior lobe hormones are produced by neurons or cells in the hypothalamus. The posterior lobe proper composed of terminal nerve endings only stores and releases the oxytocin and vasopressin. The posterior pituitary gland, or neurohypophysis, of the goat contains 10 to 15 units and a cow gland contains 30 to 40 units or more of oxytocin.²⁶ The half-life of oxytocin or vasopressin in the body is short, only 1 to 2 minutes. However, there are forms of ADH that slowly release small amounts after injection to control diabetes insipidus. The posterior lobe cells filled with a fine granular material,

release into the blood stream, by means of cell processes extending into the posterior lobe, the hormone represented by this granular material. This is an anatomical means of passing the hormone through the blood-brain barrier. The posterior lobe is not a distinct organ or gland but is a collection of terminal cell processes which store and release the hormone produced by the cells in the hypothalamus.^{6,8}

The principal use of oxytocin is to hasten the contraction and involution of the uterus after a dystocia or prolapse of the uterus. When used immediately after parturition, it may be of some value in the prevention of retained placenta. If oxytocin is to be used, it is essential that it be administered soon after parturition since by 48 to 72 hours the effects are slight as compared to the marked contractions produced within 12 hours or so after parturition when the uterus is still sensitized by the presence of many oxytocin receptors stimulated to develop by the estrogens produced by the placenta late in pregnancy.¹² For hastening involution of the uterus, oxytocin is superior to "Lentin" or the other ecbolics with the possible exception of ergonovine which acts more slowly. Oxytocin causes contraction of the smooth muscle or myoepithelial cells in the alveoli of the udder, to produce milk ejection or "let down" in heifers or cows that because of pain or for other reasons refuse to "let down" their milk even after stimulation of the udder by massage. The term "let down" is probably not proper because it infers the cow has voluntary control of milk ejection which she does not have. If 10 units or more are given intravenously the action is very rapid, with prompt "let down" within 30 to 60 seconds. Within this time the intra-cistern pressure increases from 30 to 40 mm to 60 to 70 mm of Hg. Under natural conditions, fright, pain or excitement apparently antagonizes, slows, or prevents the release of oxytocin by the posterior pituitary gland by a central nervous system block to oxytocin release or possibly by the release of epinephrine which causes a vasoconstriction preventing oxytocin from reaching the myoepithelial cells. In sheep and goats oxytocin release and milk ejection is not necessary for satisfactory milking.

The Ovarian Hormones

The hormones produced by the ovaries are: the estrogens, the progestogens, the androgens, and a nonsteroid hormone, relaxin. The first three are steroid hormones that are also produced by testes, adrenal cortices, and the placenta.^{13,30} The precursor for all steroids is pregnenolone which is derived from cholesterol.⁶ The further

biosynthesis of the steroid hormones proceeds to progesterone—testosterone—estradiol—estrone. In the circulation the steroids appear to be bound to binding proteins or globulins. The steroids are inactivated in the liver by conjugation.

The estrogens are steroid substances with the ability to produce estrum when injected parenterally into female animals, even in the spayed female. **Estradiol** and **estrone** are the natural biologic estrogens produced in animals by the cells of the theca interna of the Graafian follicle or the placenta.² The follicular fluid of a mature bovine Graafian follicle contains about 50 to 90 micrograms of estradiol per 100 ml of fluid. The amount of fluid averages 2 to 3 ml. per follicle. Estradiol from the Graafian follicle produces the clinical signs of estrum in the domestic animal. These include growth and keratinization of the vaginal epithelium, especially in bitches and queens, increased vascularity, edema, and growth of the endometrium, uterus and cervix, and increased sensitivity and amplitude of contraction of the uterine muscles. Under its influence the cervix relaxes and goblet cells in the cervix and anterior vagina secrete a large amount of clear viscid mucus in the cow and lesser amounts in the other species. The vulva relaxes and becomes edematous; this is especially noticeable in the bitch and sow. Estrogens increase the rate of migration of leucocytes into the uterine lumen and thus increases the bactericidal activity of the uterus during estrum. Thus the genital tract sensitized by the estrogens is in a state of readiness for copulation, which in turn stimulates the release of oxytocin. The greatly increased uterine contractions and characteristic mucus of estrum favor the rapid transfer of spermatozoa to the pavilion of the oviduct, and the viability and capacitation of the spermatozoa in the female reproductive tract. Certain reproductive tissues can't grow unless stimulated by estrogen. The uterus, vagina and mammary gland are tissues that are hormone dependent. Acting through the central nervous system, estradiol produces the typical clinical signs of estrum, including the female's acceptance of the male. Gonadal hormones not only bring sexual behavior to expression at estrus they also produce a differentiation or organization of neural tissues, before or soon after birth, that establishes the basic femininity, or masculinity of the individual animal.⁴³

Estradiol is responsible for the secondary sex characteristics of the female. It causes the growth of the duct system of the mammary gland. It has a definite effect on the deposition and distribution of body fat and it hastens the ossification of the epiphyses of the bones. Near the time of ovulation estradiol reaches a high enough level in the body to suppress FSH production and by

stimulating the release of GnRH and LH promotes ovulation.^{3,8} The high level of estrogens in the plasma of pregnant sows between 20 and 30 days of gestation comes from the blastocysts.^{3,6} During pregnancy the placenta produces an increasing amount of estrogen, especially the last several weeks before parturition that promotes the rapid growth of oxytocin receptors in the myometrium and mammary gland.¹² At this period estrogen initiates uterine tonus by stimulating the release of prostaglandins F_{2a} and potentiates the effects of the latter and oxytocin on uterine contractions,⁶ sensitizes the uterine muscle to oxytocin, relaxes the cervix, vagina and vulva, and the pelvic ligaments. Following parturition the level of estrogens drops rapidly. Estrogens are secreted in increasing amounts in the urine of the mare after 100 to 120 days of gestation as estrone and estriol and other forms. These are recovered as a commercial, biologic source of estrogens. The major urinary estrogen excreted in the cow is estradiol.³⁰ During gestation the action of a low physiologic level of estrogens on the pituitary gland may be necessary to help maintain the corpus luteum by stimulating the release of LH. The presence of progesterone during pregnancy prevents the occurrence of estrum.²

Being steroid in nature, the estrogens are soluble in oil and therefore are usually administered intramuscularly or subcutaneously. Estrogens may be implanted subcutaneously or intramuscularly in the form of a pellet, from which the estrogens are absorbed slowly over a period of several months. To be successful, this procedure requires a nearly sterile technique because if infection is introduced excessive connective tissue is built up around the pellet and absorption might be prevented. Other estrogenic preparations for injection are the aqueous suspension of fine particles of estrogen and the solution of estrogens in an alcoholic base or "Repositol" which precipitate when injected into the body tissues or come in contact with water. Following intramuscular injections of the aqueous suspension and "Repositol" products the fluid is rapidly absorbed, leaving fine particles of estrogen as a modified type of implant. These preparations are easier to administer but due to the fine size of the estrogenic particle it is absorbed faster than when in pellet form. Consequently injections must be repeated about every 5 to 10 days. The esterification of an estrogen will also reduce its rate of absorption and thus prolong its action. For example, the effects of stilbestrol in oil last 24 to 36 hours while the effects of estradiol dipropionate will last 24 to 48 hours and estradiolcyclopentylpropionate in oil, "E.C.P." (Upjohn) and estradiol valerate (Squibb) are effective over a period of 72 to possibly 96 hours or longer. In humans and animals

with a simple stomach, such as the dog and cat, the estrogens, like stilbestrol, may also be administered orally. Low levels of estrogens, such as 10 mg/day of stilbestrol, added to the ration of feeder cattle and sheep will increase the rate of gain and growth compared to rations not containing this hormone. The naturally-occurring estrogen, estradiol, is more rapidly destroyed than is stilbestrol when given orally.¹¹ All animals can absorb estrogens fed in their ration. Estrogens may be applied by inunctions and absorbed through the skin or from the uterus after intrauterine infusions.

There were formerly two types of estrogens available commercially; the naturally-occurring estrogens such as estradiol, estrone and estriol produced from natural sources such as the urine of pregnant mares and women, from the adrenals and testes of stallions and from the human placenta and amniotic fluid; and stilbestrol or diethylstilbestrol synthesized from various coal-tar derivatives and other steroids. Presently all types of estrogenic compounds are synthesized chemically for commercial purposes. In animals both compounds, estradiol and stilbestrol, are equally effective and desirable. While in humans estradiol is preferred because there are fewer undesirable side reactions. Milligram for milligram estradiol is about 10 times as potent as stilbestrol. Therefore a 50 mg. injection of stilbestrol is approximately equivalent to a 5 mg injection of estradiol. The U.S. Food and Drug Administration has banned the use of stilbestrol and other estrogenic growth promotants because of public health implications. A few steroidal nonestrogenic compounds as implants have been cleared for this latter use in animals.

The estrogens are probably the most widely-used hormones in veterinary medicine. They are used to evacuate the uterus in cases of a mummified fetus or pyometra in cattle, and to produce therapeutic abortion in all species. By increasing the uterine blood supply, increasing the contraction of the uterine muscles, and stimulating epithelial growth and the flow of mucus they aid in the treatment of such conditions as postpartum metritis and retained placenta. Estrogens have been shown to have a definite effect on the uterus and uterine infection by their ability to prevent, reduce, and overcome infection in the uterine cavity^{2,35} by their action on stimulating the passage of leucocytes and bactericidal substances from the leucocytes into the uterus.^{9,22,23} When administered soon after an undesired service, estrogens prevent conception by their effect on the oviduct and uterus and the transport of the fertilized ova by either tubal "locking" of ova or the expulsion, death or failure of implantation of the early embryo. All of these effects on the tubular portion of the genital tract characterize the action of estrogens.

The estrogens have also been used widely to produce signs of estrus in anestrus animals. This action is to be expected since proper doses of estrogens produce estrus or acceptance of the male even in spayed females. This artificial estrus cannot be regarded as physiological since ovulation does not occur unless the estrogen is given at the time in the estrous cycle at which ovulation would normally occur. Large or moderate doses of estrogens given at the time of estrus or ovulation often cause infertility because of their adverse effects on ova transport. Injection of estrogens in large doses over a period of time in virgin heifers or dry cows usually produces varying degrees of mammary development and lactation. The peak of production following the estrogenic initiation of lactation follows a week or two after the estrogen is withdrawn and milking has begun. This phenomenon is also observed occasionally in the natural state in newborn heifers and prepubertal heifers due to excessive assimilation of estrogens from the placenta or production of estrogen by the endocrine glands. Large doses of estrogen after parturition inhibit lactation and relieve congestion of the udder. It is also used in bitches at the end of their pseudo-pregnant period to relieve udder congestion and possibly other symptoms of pseudocyesis. Because of its effect on the muscles and epithelium of the genito-urinary system it is used in low doses in dogs affected with urinary incontinence. The estrogens are occasionally used in ointment form for their stimulating effect on epithelial tissues in obscure skin ailments or to produce cornification of the vaginal epithelium in certain types of vaginitis.

Excessive, prolonged or improper dosing with estrogens will produce cystic ovaries or nymphomania in cattle, abortion, atrophy of the ovaries and cessation of the estrous cycles. In cattle and sheep estrogens will cause the regression of the corpus luteum probably by suppressing LH secretion, by exhausting the LH levels in the adenohypophysis or by stimulating the release of prostaglandins. In the sow and horse estrogens prolong the life of the corpus luteum. Large amounts of estrogen produce edema of the vulva, excessive relaxation of the pelvic ligaments and other supporting structures, predisposing to prolapse of the vagina and rectum, and fractures of the pelvic bones. In the bitch excessive or prolonged doses of estrogens can produce a fatal anemia due to their toxic effect on bone marrow or cause cystic endometrial hyperplasia with secondary metritis and pyometra.

In animals the level of the gonadotropins in the pituitary, the length of the heat period, and estrogen threshold and excretion during estrus are strikingly parallel. The following order, from high to low is reported:

man, horse, hog, sheep and cow.²

Progesterone or the corpus luteum hormone, is a steroid hormone produced by the granulosa cells and by the corpus luteum. In many species the secretion of progesterone by the follicle begins before ovulation occurs¹³ and is continued by the mature corpus luteum since the half-life of progesterone in the blood is only 3 to 5 minutes^{8,17a,24,27} in cows and mares. Progesterone is also produced by the adrenal cortex and the placenta. Following ovulation the corpus luteum develops from the granulosa cells of the Graafian follicle and is maintained by the luteinizing (LH), luteotrophic or gonadotropic hormone of the anterior pituitary gland.^{9,39} Under the stimulation of the luteotropic hormone, the lutein cells produce progesterone. Progesterone secretion by the corpus luteum regulates the estrous cycle by inhibiting estrus and the ovulatory surge of LH and plays other important roles in the reproduction of domestic animals.³⁹ The corpus luteum is essential throughout pregnancy in the cow, doe, sow and bitch but for less than full term in the mare, queen and ewe. In these latter species the progesterone produced by the placenta maintains the latter stages of pregnancy.¹⁸

Progesterone causes the growth of the glandular system of the endometrium of the uterus and the uterine secretions ("milk") from the endometrial glands for the nutrition of the ovum, and the attachment of the embryo. It maintains pregnancy by producing a favorable environment for the survival of the developing embryo and inhibiting the motility of the uterus. By causing an inhibition of the LH and FSH or gonadotropic hormones from the anterior pituitary gland, it prevents estrus, ovulation, and the occurrence of the estrous cycle and maintains pregnancy. However enough FSH is released so that follicles may form even during the luteal phase of the estrous cycle, and also during early gestation in some domestic animals especially the mare. Even ovulation often occurs during these two periods in the mare. Research has indicated that progesterone may act with estrogen to stimulate ovulation by promoting the release of LH.³ Small amounts of progesterone injected during early estrus in the cow hasten ovulation.²⁰ Progesterone probably acts with estrogen in most species to cause signs of estrus and acceptance. If progesterone from a previous corpus luteum is lacking, the first ovulation is usually characterized by a "silent" heat. This is seen in the early part of the breeding season in sheep, in prepubertal heifers, and in the postpartum period in the cow.⁸ The endometrium and uterus, when under the influence of progesterone during the luteal phase of the cycle, are much more susceptible to infection and provide a favorable environment for bacterial development.^{2,35} Pro-

gesterone causes the development of the alveolar system of the udder. Following the first half of the period of pregnancy in women and in animals such as the mare and ewe, progesterone for the maintenance of pregnancy is produced by the placenta, and the corpus luteum becomes small and inactive. In other species, such as the cow, sow and doe, the corpus luteum is essential during most if not the entire period of pregnancy in order to prevent abortion inasmuch as apparently little progesterone is secreted by the placenta.³⁹ Because of its ability to inhibit keratinization of the vagina, to prevent sensitization of the uterus, and to prevent estrus, progesterone secreted by the placenta and corpus luteum prevents or possibly counteracts the action of estradiol also produced in large amounts during late pregnancy. In the nonpregnant bitch and queen progesterone produces changes characteristic of pseudopregnancy. The radioimmunoassay is a highly sensitive test for progesterone in milk and plasma that has been described under pregnancy tests in cows, does and mares (see Chapter II). This test is quite accurate at 21 to 23 days post service especially in nonpregnant cows. Progesterone concentrations in dairy products are associated with the milk fat levels.¹⁷

Progesterone is produced synthetically. Progesterone is prepared in an oily base, in a "Repositol" form, or in finely-divided particles in an aqueous base. The oily preparation is effective for 24 to 48 hours when injected intramuscularly; while the latter preparations are effective for about 3 to 7 days since the finely divided particles precipitate in the tissues.

Progesterone is used to prevent or control habitual abortion due to an actual or possible progesterone deficiency. It may be used to promote conception the first 20 days of gestation in the cow. In the mare, ewe, cow, sow, bitch and queen, progesterone or synthetic progestogens can be injected or fed orally and prevent estrus from occurring by suppressing the release of the gonadotropic hormones, for as long as the injections or feeding are continued.³⁹ However, conception rates at the estrus following its withdrawal have been lower than in non-treated animals. Progesterone has been used experimentally to maintain pregnancy in animals in which the corpora lutea have been removed. If injections are continued beyond the normal length of gestation, prolonged gestation and fetal death may result. Progesterone has a "calming or tranquilizing" as well as an antiandrogenic effect and has been used for a variety of aggressive or antisocial behavior problems in dogs, cats, mares and stallions by the author and others.²¹

Relaxin is a water-soluble polypeptide hormone apparently present in the ovaries, probably the corpus lu-

teum, placenta and uterus during the late stages of gestation and is responsible, along with estrogen, for the relaxation of the pelvic ligaments and cervix necessary for parturition in sows, ewes, cows and possibly dogs.^{3,5,8} In the pregnant guinea pig and gopher it is able to cause resorption of the pelvic symphysis. This relaxation effect is brought about by an enzymatic depolymerization of the ground substance or collagen.

Prostaglandin (PG) was first described in 1934 after it was found in human semen. Prostaglandins are potent biologic agents found in many body tissues. Since they usually act locally, they don't usually conform to the classic definition of a hormone. Phospholipids in cell membranes give rise to arachidonic acid, a fatty acid which is the precursor for the major prostaglandins F_{2a} and E_2 . Glucocorticoids can inhibit the formation of arachidonic acid from phospholipids. Aspirin, phenylbutazone and other nonsteroidal anti-inflammatory agents can inhibit the formation of prostaglandins from arachidonic acid. Other important and highly active metabolites of the arachidonic cascade^{2a,11,19} are the thromboxanes, prostacyclins, and the leukotrienes that, together with the prostaglandins, produce a variety of effects on the reproductive, circulatory, respiratory and other systems and cause inflammatory reactions in joints and other tissues. Prostaglandins are even present in the corpus luteum.¹⁹

Prostaglandins play a number of important roles in reproduction including: gonadotropin release, ovulation in certain species, regression or luteolysis of the corpus luteum to control the estrous cycle, produce uterine motility and contraction, oxytocic effects, at parturition and in sperm transport.^{3,5,8,11,39b} Prostaglandins are also involved in cervical "ripening" and relaxation at the time of parturition in mares, ewes and women. In the periparturient sow postaglandin (PGF_{2a}) is released from the placenta and uterus causing luteolysis of the corpus luteum and a decline in plasma progesterone together with a marked rise in relaxin, and a further rise in prolactin and estradiol.^{25a} In most large domestic animals prostaglandin is elevated for a number of hours before parturition but in the mare its elevation closely coincides with delivery.¹¹

The uterine prostaglandins are produced by the endometrium from arachidonic acid under the influence of estrogens and oxytocin. The regulation of the estrous cycle by the luteolytic effect of the uterine formation of prostaglandin is a complex mechanism that differs between species. Prostaglandins are short-lived and after they enter the general circulation they are metabolized very rapidly by enzyme action. The prostaglandins used for luteolysis and estrus synchronization have no effect on the

ovum, ovulation, sperm cells or the fertility of the subsequent breeding that occurs 2 or 3 to 10 days after the injection in the mare, cow, ewe and doe.¹¹ The prostaglandins do not cause luteolysis in sows until after the twelfth day of the estrous cycle⁸ and they are even more limited in value in the bitch and queen for synchronizing estrus.

After ovulation in the cow, ewe, sow and mare the corpus luteum matures rapidly and produces progesterone that prevents estrus for the duration of the cycle. Prostaglandins can only cause luteolysis of the mature corpus luteum after about the fifth or sixth day after ovulation in the cycling cow, doe, mare and ewe. In the cow, ewe and doe, endogenous prostaglandin F_{2a} from the endometrium travels to the corpus luteum by passing from the uterine vein to the ovarian artery which lie in close apposition. In the cow one-fifth of the required systemic dose of prostaglandin if infused into the uterus will cause luteolysis by this local pathway.²⁸ In the mare this local venoarterial pathway is not present so prostaglandin from the endometrium reaches the corpus luteum by the systemic circulation. In both instances the prostaglandin constricts the blood supply to the corpus luteum and acts directly on the luteal cells to produce luteolysis.^{5,8,6,11,17b,19,28} If the animal conceives then the early embryo or blastocyst secretes hormones or substances that prevents the formation of prostaglandins in the endometrium and maintains pregnancy by the persistence of the corpus luteum, often called "maternal recognition of pregnancy." Similar persistence of the corpus luteum is observed in chronic uterine infections or pyometra,^{39b} hysterectomy performed during the luteal phase of the cycle and in rare cases of congenital hypoplasia of the endometrium and caruncular areas in heifers in which the endometrium is unable to produce prostaglandins.

A number of techniques or agents have been shown to induce the secretion of prostaglandins in cycling and even pregnant animals and cause the involution or luteolysis of the mature corpus luteum. In the mare these include: manual dilation and manipulation of the cervix, natural breeding of a mare after administering a large dose of estrogen, douching the uterus with 500 ml. or more of physiological saline^{5,39b} and taking an endometrial biopsy. These techniques probably stimulate the release of prostaglandin by the equine endometrium and a normal estrus occurs within 3 to 10 days. In the cow these procedures include: injecting daily doses of oxytocin between the second and sixth day of the cycle,^{8,19,39b} injecting 5 to 10 mg. of estradiol valerate when a mature corpus luteum is present either during an estrous cycle or during early pregnancy, introducing an infectious agent, an irritating solution such as weak Lugol's iodine or an

intrauterine device (IUD) within a few days after estrus and the resulting stimulation of the endometrium causes a release of prostaglandin and the development of a short 8 to 10 day estrous cycle. It is possible that in exogenous estrogen therapy that LH release from the anterior pituitary gland is also suppressed. It is also possible the introduction agents into the uterus or dilating the cervix introduces bacteria from the caudal reproductive tract into the uterus resulting in endometritis and prostaglandin release.

A number of stable prostaglandins (PGs) and their analogues have been produced commercially and are used therapeutically to cause luteolysis of the mature corpus luteum after the fifth or sixth day postovulation to produce estrus or estrus synchronization or abortion in the mare, cow, ewe, doe and sow.^{3,4,39b,40} (See Chapter V.) Prostaglandins are not effective when the corpus luteum is immature and developing. PGs are also used to evacuate the contents of the uterus in pyometra of the cow and bitch, and a mummified bovine fetus. Prostaglandins are also used, especially in sows, to induce parturition (See Chapter VI) and to treat "persistent" corpora lutea or "pseudopregnancy" in mares.^{11,39b} The prostaglandins available commercially have now been officially approved for use in lactating dairy cows. These products include: "**Prostin**," "**Lutalyse**" from Upjohn Company which is prostaglandin F_{2a} (dinoprost tromethamine) for mares and cows, respectively, with suggested doses of 5 to 15 mg. (10 mg.) for mares, 15 to 35 mg. (25mg.) for cows, and 7 to 15 mg. (10 mg.) or less in ewes, does^{11,33} and sows. In mares this product causes mild to moderate side-effects lasting for up to one hour of sweating, increased heart and respiratory rate, defecation, urination and discomfort due to increased peristalsis.^{28b} Other prostaglandin analogues that do not cause these side-effects include: "**Equimate**" (fluprostenol, ICI 81,008) from Haver Lockhart Lab with a dose rate for mares of 250 ug; "**Synchrocept**" (prostaglandin, RS 9390) from Diamond Lab with an equine dose rate of 2 mg., and "**Estrumate**" (cloprostenol, ICI, 80996) presently from Imperial Chemical Industries with a bovine dose rate of 500 ug. and for ewes and does 125 ug.

After the injection of prostaglandins into mares, cows, and ewes or does that are cycling normally and have a mature corpus luteum, after 5 to 7 days postestrus, the corpus luteum regresses and a normal fertile estrus usually occurs. In mares this is 3 to 12 days later with most mares showing estrus within 2 to 5 days and ovulation 6 to 12 days after the injection. In ewes and does estrus usually occurs 2 to 3 days post injection.³³ In cows estrus usually occurs 2 to 5 days later or at about the same time as they would if the corpus luteum had been expressed

manually.^{5,6,8,11,19} Estrus synchronization is generally more precise after two treatments with prostaglandins, in the mare 12 to 14 days apart, in the cow 10 to 12 days apart, in does 11 days apart and in sheep 8 to 11 days apart. In mares 2,500 IU of HCG may be injected 6 days after the prostaglandin to promote or "pinpoint" ovulation which usually occurs 24 to 48 hours later.¹¹

Other Endocrine Glands

Other endocrine glands that are associated with reproduction are the thyroid, adrenal, and the pineal gland. Pheromones also exert endocrine effects on reproduction.

The thyroid gland secretes thyroxine and triiodothyronine, composed of iodinated amino acids, under the regulation of the thyrotropic or thyroid stimulating hormone from the basophilic beta cells in the anterior pituitary gland after release by TRH from the hypothalamus. Thyroxine and triiodothyronine have been synthesized. The latter is more active and potent.¹³ The thyroid gland contains large amounts of iodine. In humans hypothyroidism is believed by many to be associated with sterility, infertility and abortion. Thyroid activity is necessary for normal reproductive functions. In the United States thyroid abnormalities such as goiter are most common in the iodine-deficient areas around the Great Lakes and the northeastern part of the country. Goiter or an enlarged thyroid is produced by excessive stimulation of the thyroid gland by TSH when the gland cannot meet the body's need for thyroxine. Hypothyroidism causes a low metabolic rate that is believed to have an adverse effect on human fertility and pregnancy and often is associated with obesity.

Since thyroxine and triiodothyronine are quite expensive when obtained from animal sources or synthesized, and because there has been little work to show the need of these in various sterility or impotency problems in animals, its use is limited. Some veterinarians have indicated thyroprotein may benefit males and even females that lack libido. This could be related to overconditioning. An iodinated casein was developed with about a 3-percent thyroxine potency. "Protamone" contained thyroxine and triiodothyronine.⁸ This has been marketed by the Cerophyll Laboratories in Kansas City, Missouri. In daily doses of 1 gm per 100 lbs. of weight it may be fed to livestock, in which it produces a definite increase in the basal metabolic rate, as shown by an increase of 5 to 20 percent in milk production together with a higher percentage of milk fat in lactating dairy animals (Chapter IV). Because of the cost, dangers and restrictions associated with its feeding to increase milk production, the use of thyroprotein has been limited. It causes a marked

loss in weight in fat animals. Preliminary clinical studies in cattle suggest thyroprotein or triiodothyronine may be of value in certain types of female infertility such as "silent" estrus,⁸ or prolonged infertility associated with a steer-like appearance. In males, especially old, fat males, it may increase their activity and reduce their weight. In some males this may result in some improvement in sexual desire. However, the same purpose can usually be accomplished by restricting the rations and increasing exercise. The use of iodinated casein for reproductive diseases in livestock appears limited. Thyroid function tests are now available, although costly, for domestic animals.⁸

The adrenal gland, composed of the medullary and cortical portions, secrete hormones that have profound effects on other body systems and functions and thus may indirectly affect reproduction.⁴¹

The adrenal medulla secretes adrenalin, or epinephrine, which has been synthesized; it is protein in nature and water-soluble. This hormone stimulates the sympathetic nerves, whether the sympathetic nerve of the organ is excitatory or inhibitory. In cows adrenalin may prevent the normal "let down" of milk by preventing oxytocin release from the posterior pituitary lobe. It causes a relaxation of the estrogenized uterine muscle in the cow. In other species it may cause contraction of the gravid or nongravid uterus. Epinephrine has been used by some veterinarians to control hemorrhage following the manual removal of the corpus luteum in the cow, but there is no pharmacologic justification for its use in this condition.

The adrenal cortex secretes steroidal hormones, such as corticosterone or cortisol that control glycogenic activity and protects the individual against various stresses, and desoxycorticosterone or mineralo-corticoids that control electrolyte and water metabolism. These hormones have no direct effect on the reproductive organs but glucocorticoids in moderate or large doses may cause abortion or premature birth, especially late in gestation in the cow, ewe and doe. The adrenal cortex, which originates from mesodermal cells closely related to the embryonic gonadal cells,⁴¹ secretes androgens, estrogens and progesterone in small amounts.⁸ Progesterone is a precursor of cortisol. Stress factors on the female cause an increased secretion of cortisol mediated by CRH from the hypothalamus and ACTH from the anterior pituitary gland. Transport stress significantly increased the occurrence of estrus in sows.⁴¹ Increased ACTH may be a factor in the cause of bovine cystic ovaries. High levels of cortisol from the fetal adrenals is closely associated with the onset of parturition in the cow and ewe. In rare instances tumors of the adrenal cortex may secrete sufficient androgens to cause masculinization or virilism in

a female. In the cow, because of the increased demands of the body for cortical hormones during gestation and the first third of the lactation period, the adrenal cortex is usually larger than normal for that length of time.

The pineal gland or body, attached in most animals by a short-stalk to the roof of the third ventricle of the brain is thought to be an endocrine gland in animals like the horse and sheep that are seasonal breeders. Current reviews^{5,6} reported that although much more research is necessary, evidence indicates that the pineal gland, stimulated by light by neural pathways from the eye, may secrete melatonin or a polypeptide. In mares melatonin acts as an inhibitor, or in ewes^{32b} as a stimulator of the gonadotropic centers of the hypothalamus to regulate the breeding season in these photoperiodic species. Intramuscular injection of 2.5 mg of melatonin daily into ewes hastened the onset of the fall breeding season or extended the length of the breeding season in the spring.^{32b}

Pheromones are odoriferous substances, external "chemical messengers," that, although they don't meet the definition of a hormone, serve as communication media between animals.^{5,8} The sex pheromones come from modified skin glands like the preputial glands in the boar and the glands at the base of the horns in bucks. The urine apparently contains pheromones in dogs, cattle, swine and sheep, as well as saliva in boars, as do other skin glands of the external genitalia and other body regions in the dog and horse. The development of these pheromones occurs with puberty and the production of estrogens and testosterone. A pheromone present in the vaginal secretion of bitches in estrus that attracts dogs and stimulates them to mount the bitch is methyl p-hydroxybenzoate.^{18b} The flehmen stance observed in horses, and ruminants is believed to provide the vomeronasal organs, with their sensitive odor receptors in the nasal passages, concentrated pheromone laden air from the urine or perineal region by closing the external nares. Tongue movements in cattle prior to the flehmen stance may force fluids, that often contain urine from estrous females being "teased," from the oral cavity into the incisive pits and fissures and into vomeronasal organ.^{25a} These olfactory stimuli along with other acoustical, visual and tactile stimuli provide both the female and male animals information on the sexual state of the other that is transmitted to the brain and hypothalamus. These odors present at estrus can be recognized by other species.^{25b}

The hormones concerned with reproduction in the male animal are described in Chapter XVIII.

Puberty

Puberty may be defined as the age or time at which the generative organs become functional and reproduc-

tion may occur. Puberty does not signify full or normal reproductive capacity, which develops later. In the male, puberty is indicated, along with other secondary sex changes, by the ability to copulate and produce sperm. In the female animal, it is characterized by the appearance of estrus and ovulation. The time of onset of puberty in animals is greatly modified by environmental and genetic factors. A high plane of nutrition hastens the onset of estrus especially in cattle and horses. A low plane of nutrition or deficiencies of various nutrients as well as disease factors will delay puberty. Exposure to stress conditions especially during the cold months of the year delay the onset of puberty. In certain animals such as sheep which have a limited breeding season puberty does not occur until that season, at which time the animal may be nearly fully grown. Inbreeding tends to delay puberty while crossbreeding tends to hasten its occurrence. Brahman and Zebu cattle reach puberty 6 to 12 months later than the European (*Bos taurus*) breeds. The larger breeds of cattle and horses tend to have a later onset of puberty than the smaller breeds.^{3,6,8,4,6,15,16} The age at puberty was less variable than the weight in gilts on a high and low plane of nutrition. In 3 groups of 21 calves each, fed on the following three levels of nutrition, 140 percent, 100 percent, and 60 percent, as based on Morrison's standards,^{13,14} the heifers on the high level of nutrition reached puberty with the first estrus at an average of 37.4 weeks of age weighing 580 lbs., the heifers on the average level of nutrition reached puberty at 47 weeks of age weighing 597 lbs., and heifers on the low level reached puberty at 65 weeks weighing 502 lbs.

The attainment of puberty is a slow, gradual process. Graafian follicles must attain a fairly advanced stage of development before the gonadotropins are effective. Puberty depends upon the release of the gonadotropic hormones from the anterior pituitary gland. Injection of these hormones into prepubertal animals may cause precocious sexual maturity. The gradual nature of the processes leading to puberty is cited in the human, in which secondary sex characteristics develop before menstruation occurs, and menstruation takes place for a period of time before ovulation occurs.^{2,1} In 53 Holstein heifers with a mean interval from birth to the first ovulation of 296 days and a mean weight of 609 lbs, "silent" estrus was exhibited in 74 percent of the heifers at the time of their first ovulation.⁷

Puberty in most of our domestic animals, especially those reared and fed under the most artificial conditions occurs much earlier than does sexual maturity or full or normal reproductive capacity. Most animals that normally give birth to 2 or more young at a time are less fecund immediately after puberty than they are later.^{2,1}

Yearling ewes usually have only one lamb. Primiparous gilts usually have smaller litters than 2- to 4-year-old sows. Fertility denotes the ability to produce young, while fecundity denotes the number of young produced. Fertility is reached at puberty but fecundity increases with age to maturity and then later in life decreases. Early fertility and high initial fecundity usually indicates that an animal will have a good reproductive record in the future.

Because of environmental influences, frequently estrum occurs at such an early age that if conception occurred parturition would be disastrous due to the small size and lack of development of the dam. Young female animals should not be bred until their body development ensures a normal gestation and parturition. Heifers should probably be bred according to size and weight rather than by their age. Puberty is more closely related to weight than age in domestic animals, except swine. Dairy cattle usually reach puberty when their body weight is 30 to 40 percent of adult weight, beef cattle 45 to 55 percent and sheep 40 to 60 percent of adult weight.⁶ Small breeds reach puberty earlier than large breeds.⁸ It has been recommended that Holstein and Brown Swiss heifers not be bred until they weigh about 750 lbs., Ayrshires about 650 lbs., Guernseys about 550 lbs., and Jerseys about 500 lbs.⁹ Heifers may reach this size from 10 to 24 months of age depending upon feeding levels and management practices. Rapid pubertal growth in Holstein heifers started during the seventh month after birth. By the tenth month this rapid growth of the genital tract terminated and subsequent growth was much slower.³ By proper feeding and management it may be possible by early breeding of heifers at 10 to 15 months of age and mares at 2 years of age to produce one additional calf or foal per female.

At the onset of puberty the gonadotropic hormone levels rise due to an increase in amplitude and frequency of periodic pulses or releases from the anterior pituitary gland. This rise is followed by gradual increases in levels of the gonadal steroids, estrogens and testosterone. Antral follicles must have formed to get this latter response in the female. Ovulation requires a high level of estrogen to cause an LH or gonadotropic surge.⁶ In the cow and ewe and possibly the mare, a "silent" estrus and ovulation may precede the first observed estrus.^{3,8} Some workers believe a small amount of progesterone from a regressing corpus luteum is necessary along with the estrogen from a mature follicle to produce psychic estrus.⁸ Based on rectal palpation and careful observation of 37 peripuberal heifers,⁸ signs of behavioral and physiological estrus without standing for mounting and without ovulation were observed 38 times before the first standing estrus. The cycles were all the same approxi-

mate duration, 20 days, despite the following conditions. Of the 245 cycles studied 7 percent had a silent estrus, 25 percent had a nonstanding estrus and 68 percent had a standing estrus. Anovulation occurred in 14 percent of the cycles, cystic follicles in 11 percent, cystic corpora lutea in 14 percent and normal corpora lutea in 61 percent of the cycles. Anovulation was associated with the signs of first estrus in nearly 50 percent of the heifers and then declined rapidly at subsequent cycles. Some anovulatory follicles progressed to cystic follicles. A normal corpus luteum was detected at the first estrus in 35 percent of the heifers and increased in subsequent cycles. Thus anovulation may be responsible for failure of conception.

Control of puberty in animals is presently largely limited to nutritional and environmental factors. Other lesser factors might include control of the photoperiod in seasonal breeders, heterosis or breed selection and social-sexual interactions between males and pubertal females. The hastening of the onset of puberty in gilts and possibly heifers by the presence of males is largely conditioned by the male sexual odor or pheromone present in the urine and by stimulation of the hypothalamic-pituitary axis.^{5a,b} The use of sex steroids and gonadotropic hormones to hasten the onset of puberty have not as yet proven to be practical or successful.^{2,5}

The onset of puberty in the domestic animals is as follows:

Horses—10 to 24 months, average 18 months of age, depending on the breeding season.

Cattle—6 to 18 months. Heifers in rare instances may come in estrum as early as 3–4 months of age, or if kept in a cold environment on a low level of nutrition, the first estrum may not occur until 24 months of age. In Brahman heifers puberty occurs at 19 to 27 months of age.¹⁵

Sheep—6 to 12 months, usually in the fall but depending on the breeding season.

Swine—5 to 8 months, average 6 months.

Dogs—6 to 12 months, average 7 to 10 months.

Cats—6 to 16 months, average 11 to 12 months, depending on the breeding season.³

Since puberty occurs before conception, normal gestation and parturition can take place, most well-grown dairy heifers are not bred until they are 14 to 18 months of age. Beef and poorly-grown dairy heifers may be bred from 18 to 24 months of age. Fillies should not be bred until 2, or preferably 3, years of age. Gilts, unless well grown, should not be bred before they are 8 to 9 months of age. Ewe lambs under 12 months of age should not be bred. It is generally considered undesirable to breed bitches on their first estrum or bitches or queens before

they are a year old. Following breeding of the pubertal animal, the nutritive level during the first gestation should be adequate to continue normal growth and development so by the time of parturition complications such as dystocia do not occur.

The Estrous Cycle

In all species of domestic animals that have reached puberty there is a definite physiologic functional rhythm of the reproductive system, called the estrous cycle. Although each species has its own peculiarities regarding their estrous cycle pattern, basically all are similar. The estrous cycle lasts 16 to 17 days in the ewe, 20 to 21 days in the cow, doe and sow and 21 to 23 days in the mare.⁶ The estrous cycle is commonly divided into 4 phases or periods that blend one into the other. Some authors prefer to divide the estrous cycle into two periods the **estrogenic or follicular phase** comprising proestrus and estrus and the **progestational or luteal phase** comprising metestrus and diestrus.^{3,5,6,8}

Proestrus is an ill-defined period during which the Graafian follicle is growing under the influence of FSH and producing increasing amounts of estradiol. There are increases in the growth of cells and cilia lining the oviduct, in the vascularity of the uterine mucosa, and in the thickness, edema and vascularity of the vaginal epithelium, with cornification occurring in some species, such as the bitch and queen. In the bitch, the increased endometrial vascularity is characterized by bleeding. In the bitch and sow the vulva becomes definitely edematous and swollen. There is a gradual relaxation of the cervix and an increased secretion of viscid, slimy mucus from



Figure 103. Heifer in Estrus—Standing to be Mounted.



Figure 104. Normal Genital Tract of a Heifer in Estrus—Note maturing follicle in the right ovary and regressing C. L. in the left ovary. (Courtesy K. McEntee.)

the goblet cells of the cervix and anterior vagina and from the uterine glands. In the cow and mare, the sticky, dry mucus of the preceeding period changes during proestrus to a milky, viscid mucus, and finally to a clear, transparent, stringy mucus late in the proestrous period. There is an increased excretion of estrogen in the urine and a beginning decrease of progesterone in the blood.³ The corpus luteum is undergoing rapid vacuolization, degeneration, and decrease in size in the mare, cow, ewe, doe and sow. The marked increase in growth of the epithelial tissues, of the activity of the musculature of the reproductive tract, of the secretion of mucus, and of the vascularity of the endometrium and vaginal mucosa is spoken of as the building-up period. It is produced by the secretion of increasing amounts of estradiol. Late in this phase of the cycle the female animal usually exhibits interest in the male.

Estrus is the fairly well-defined period characterized by sexual desire, immobility in the presence of, and the acceptance of the male by the female domestic animal. (See Figures 103 and 104.) This period begins with the time of the first acceptance and ends with the last acceptance of the male. During this period the female will usually seek out and accept the male. The Graafian follicle is large and mature. The ovum undergoes certain maturational changes. Estradiol from the maturing Graafian follicle produces changes in the tubular genital tract that reach their culmination in this period. The uterine tubes are tonic, the epithelium mature, and the cilia are active; contraction of the uterine tubes is occurring; and the fimbriated end of the uterine tube is assuming a close affinity to the Graafian follicle. Increased amounts

of tubal fluid is being secreted. The uterus is erect, turgid, and some species, edematous. The blood supply to the uterus is increased; the mucosa is growing rapidly, and mucus is secreted. The vaginal and cervical mucus is greatly increased. The mucosa is pink and congested, due to the increased vascularity. The cervix is relaxed and slightly edematous. The mucosa of the vagina is greatly thickened with many cornified epithelial cells being desquamated in certain species, such as the bitch and queen. The vulva is relaxed and edematous in all species, but most noticeably in the bitch and sow. Strings of mucus may hang from the vulva and tail of the cow. Toward the end of this period there may be an increase in leucocytes migrating into the uterine lumen. In domestic animals the elevation of estrogen to a peak in the absence of progesterone triggers the release of luteinizing hormone, the LH surge, near the onset of estrus that causes ovulation a day or so later.^{3,6,8} In most species the rupture of the mature ovisac or ovulation occurs toward the end of this period of estrum. In the cow and ewe ovulation occurs about 24 to 30 hours after the onset of estrus, 35 to 45 hours in sows, 4 to 6 days in mares,⁶ 24 to 48 hours in bitches and 24 to 30 hours after coitus in the queen. In certain species that do not ovulate spontaneously, such as the cat, rabbit, and ferret, ovulation does not occur until coitus and/or mounting takes place; hence in the queen estrum may be prolonged 7 to 10 days in the absence of a male. The acceptance of the male during estrum is due to the influence of estradiol on the central nervous system, producing the characteristic behavior patterns of receptivity in the various female animals. Female as well as male sexual behavior patterns are not sex-specific and that under certain conditions each exhibits the behavior patterns of the other.¹³

Metestrum or postestrum is a poorly defined period following estrum during which the corpus luteum grows rapidly from the granulosa cells of the ruptured follicle under the influence of the luteinizing hormone (LH) of the anterior pituitary. Metestrum is largely under the influence of progesterone produced by the corpus luteum. The presence of this hormone, by inhibiting the secretion of FSH by the pituitary gland, prevents the development of more Graafian follicles and the immediate development of another estrum. During metestrum in some species the epithelium of the vagina loses most of its new growth through desquamation. In the cow, during the early part of metestrum the epithelium over the caruncles of the uterus is very hyperemic and some capillary hemorrhage occurs. This is called postestrua or metestrua bleeding or "menstruation." This is not similar to true menstruation in primates which occurs at the time of progesterone withdrawal and is associated with a loss of the superficial layers of the endometrium. In cattle postes-

trual bleeding is associated with estrogen withdrawal. The mucous secretion decreases and the glands of the endometrium grow rapidly. Toward the middle to the end of metestrum the uterus becomes rather soft and pliable, due to a relaxation of the uterine muscle. In bitches and queens this stage includes the pseudopregnant period. In the species having diestrual cycles, including the cow, ewe, doe, sow and mare, the length of metestrum is about equal to the time it takes for the ova to reach the uterus or about 3 to 6 days. In the bitch and queen the pseudopregnant period may last about 50 to 60 days and 30 to 40 days, respectively, after which the corpora lutea regress and an anestrus of varying length occurs. In the queen that is not bred ovulation and corpus luteum development doesn't occur and the follicles become atretic. Several cycles of this sort may occur in the cat before a period of anestrus sets in. Bitches and queens do not have diestrual periods.

Diestrum is the longest phase or period of the estrous cycle in domestic animals including the cow, ewe, doe, sow and mare. The corpus luteum is mature and the effects of progesterone on the reproductive tract are marked. The endometrium becomes thicker and the glands hypertrophy. The cervix is constricted and the vaginal mucus is scant and sticky. The mucous membrane of the vagina is pale. The uterine muscle is relaxed. Late in this period the corpus luteum begins to show retrogressive changes and gradual vacuolization. The endometrium and its glands atrophy or regress in size. Beginning development of the primary and secondary follicles and finally proestrus occurs. In certain species that are not polyestrous, anestrus may occur.

Anestrus, when referred to in connection with the physiologic estrous cycle, is usually characterized by quiescent, functionless ovaries and reproductive tract. Anestrus is eventually followed by proestrus. Anestrus is observed physiologically in most mares during the winter months and in the ewe during the late spring and summer months. In the bitch and queen a physiologic anestrus period lasting several months may occur two or three times a year. The term anestrus is used, therefore, to differentiate it from diestrus, which lasts only a week or so and is characterized in the cow, sow, and other polyestrous animals by a mature corpus luteum. During anestrus in the mare the uterus is small and flaccid. The cervix is usually slight to very relaxed and the vaginal mucus is scanty and sticky. The vaginal mucosa is pale and the cervix is pale. Some follicular activity of the ovaries may develop but a mature follicle and ovulation seldom occur during the anestrus period.

The relative lengths of these various periods of the estrous cycle in domestic animals are approximately as follows:^{3,8}

	Estrum	Metestrum
Cow	12 to 24 hours	3 to 5 days
Mare	4 to 7 days	3 to 6 days
Sow	2 to 4 days	3 to 4 days
Ewe	1 to 2 days	3 to 5 days
Bitch	9 days (4-12)	
Queen	8 days without coitus ² 5 days with coitus ³	

	Diestrum	Proestrus
Cow	13 days	3 days
Mare	6 to 10 days	3 days
Sow	9 to 13 days	3 days
Ewe	7 to 10 days	2 days
Bitch	75 days (51-82) ¹	9 days (3-16)
Queen		2 days (1-3)

¹Anestrus—125 days (15-265) follows pseudopregnancy.

²Days to next estrus—14 to 21.

³Days to next estrus—42 (30-75).

(See also the Reproductive Tables at the end of this Chapter.)

Animals may be divided into three classes according to their estrous cycles. **Monestrous** animals are those animals having one estrous cycle per year. These are usually wild animals. **Polyestrous** animals are the domestic animals such as the cow, sow, and mare that have frequent periodic estrous cycles throughout the year. During the late fall and winter months the mare, especially the pony mare,⁵ usually has an anestrus period without estrous cycles. **Seasonal polyestrous** animals are those, like the ewe, that have periodic estrous cycles during only certain seasons of the year. The bitch and queen are more nearly like the monestrous animals. The bitch may have 2 to 3 periods of estrus each year. Three estrous periods per year are not uncommon in small breeds of dogs. The queen may have several heat periods in succession if coitus does not occur. These recurring episodes may occur two or three times a year. This arbitrary classification of animals as monestrous, polyestrous, and seasonally polyestrous must not be taken as entirely accurate and precise.

Excellent nutrition and environment may cause bitches to show estrus at any month in the year, and more frequently than once or twice a year. In mares, these factors may result in successful service during any month in the year. In ewes, recent work reveals a probable subclinical abortive estrual cycle present in most ewes during anestrus, especially the latter part of this phase. Certain breeds of sheep such as the Dorset and Merino regularly have

two seasonal polyestrous periods in both the spring and fall. The fall season is more fertile than the spring and summer, and a greater percentage of ewes are cycling.^{3,21} Thus the present classification may be more a clinical than an actual classification. In swine and bitches and in most queens much of the lactation period is usually characterized by a lack of estrus, termed "lactational anestrus." This postpartum, "anestrus" period is prolonged in cows nursing calves.^{5,25}

Factors Affecting the Reproductive or Estrous Cycle

Factors influencing the onset of estrous cycles of domestic animals are many and varied and irregularities, especially in the length of the cycle, are frequently observed by veterinarians and farmers. These abnormal estrous cycles may commonly be a cause of infertility. The failure of mares to have normal estrous cycles was one of the most important causes of infertility in that species.⁸ Some of these irregular estrous cycles are due to definite and known causes while others still remain to be completely explained. The causes of irregular estrous cycles include:

Nutritive state—Any severe degree of inanition or starvation caused by a lack of TDN or energy or any nutritive deficiencies, especially those causing a loss of appetite such as phosphorus, cobalt, possibly iron, copper, iodine, protein and others, may impair or prevent the secretion of gonadotropic hormones by the pituitary gland and result in a failure of the estrous cycle. In cows anestrus, possibly due to the above deficiencies, may be associated with a low P.C.V. or hemoglobin below 9 mg/100 ml. of blood. In humans it is well known that starvation causes a cessation of the estrous cycle and amenorrhea before other body disturbances appear. In rats a 15 percent loss of body weight may stop the estrous cycle. In a nutrition experiment at Cornell, in which sodium chloride was withheld from cows for long periods, the animals became very thin and cachectic and estrous cycles ceased.

Seasonal Influences and Light: Most animals in the natural or wild state are usually seasonal breeders and parturition generally occurs in the spring and summer when the weather is most favorable for the young and when food is most abundant for the dam. Although domestication has altered this pattern in some animals, the natural tendency remains.

The horse and fur-bearing animals tend to come into estrus and breed during the spring months under the influence of increasing daylight. Even in the cow, which is polyestrous, the best breeding months in the northern

hemisphere are May, June, and July and the poorest December, January, and February.¹⁸ The reverse condition is seen in ewes and does in the northern hemisphere; most breeds come into estrus under the influence of decreasing daylight and are fall breeders. This seasonal breeding trait is regulated by the effect of light, through the medium of the eyes, possibly the pineal body, the hypothalamus and the anterior pituitary gland.^{5,11,2,5,21} The effect on the animal of the total daily amount of light is important in controlling the onset of the estrous cycle and breeding season of mammals. This is called sexual photoperiodicity. A recent report on light and its effect on the gonadotropic hormones in seasonal breeders shows that the length of the daylight period necessary for sexual stimulation does not require that light must stimulate the nervous system the whole light period. Light is most efficient at only a precise period of the 24 hour daylight through dark cycle. This sensitive period varies in the different species but apparently occurs 10 to 20 hours after dawn and requires a specific period of one to several hours of light.⁶ Further study of this phenomena is indicated for sheep, horses and possibly cats.

Animals taken from one hemisphere to the other change their breeding seasons in accordance with the amount of daylight. Ewes and does confined experimentally in a darkened shed for increasing periods of time during the summer months developed estrous cycles earlier than normal. The length of estrus decreased and the length of diestrus increased in horses toward the summer months, or the end of the breeding season.⁸ Gradually increasing the total daily hours of light up to 16 hours per day by artificial means will hasten the onset of estrous cycles by 40 to 60 days in mares in the spring of the year (See Chapter XIV, Infertility in the Mare). Possibly this amount of continuous light may not be necessary. At the beginning or end of the breeding season, cycle lengths in ewes were more often longer or shorter than the average of 14 to 19 days.²⁶ Similarly in mares abnormalities of the estrous cycle are seen most commonly early in the spring during the transitional period and late in the breeding season with excessive estrous signs frequently observed early in the season. In the seasonal breeders that respond to increasing or decreasing daylight there is a refractory period that occurs at the end of the breeding season.²¹

Temperature—the influence of environmental temperature has less direct effect than has the amount of light on reproduction in animals. It has been hypothesized that excessive heat during the summer months, causing decreased thyroid activity, may indirectly reduce reproductive efficiency in swine, possibly cattle and sheep. This has also been shown to be caused by the effect of

heat on the very early developing embryo. In the bull and ram "summer sterility" is due largely to the adverse effect of prolonged atmospheric heat on spermatogenesis. Excessive exposure to cold, together with a reduced feed intake during the winter months, may cause failure of the estrous cycle in young growing animals or animals on a borderline of nutritive intake, since this intake must largely be used to maintain the animals' body temperature and necessary activities. By using a temperature-controlled room kept at a temperature of 45–48° F the onset of the estrous cycle in ewes was stimulated so they came into estrus 20 to 50 days earlier than control ewes subjected to the same amount of light but kept in summer atmospheric temperatures.¹⁰ This was also effective in improving or maintaining the fertility of rams. Estrous periods in dairy cattle in the northern half of the U.S.A. are about 18 hours long,¹⁵ while in the Gulf States they are shorter, about 12 hours.¹² It was also noted that the length of the estrous cycle in cattle under hot conditions increased to 25 days as compared to 20 to 21 day cycles in cooler weather.¹¹

Age—In cattle and swine, the young female usually has a slightly shorter length of estrus and estrous cycle than has the adult animal. The ewe lamb will not show estrus until the fall hence the sexual cycles in this species depend more upon the season than upon the pubertal age of the young female. Senility accompanied by defective teeth and marked weight loss, often results in a cessation of the estrous cycle or anestrus. Old age itself is relatively seldom a cause for reproductive failure. Senile changes, such as the menopause in women, seldom occur in animals. Whereas cessation of reproduction in women is associated with a particular age at which the oocytes in the ovaries are largely depleted, this apparently is uncommon in animals.

Character of work—Horses that are worked or raced hard frequently do not develop regular estrous cycles until the severe work schedule is stopped and they are rested, preferably on pasture for several months. Cows that are very heavy producers of milk may not have estrous cycles for 3 to 4 months or more following parturition due to a negative energy balance. Thus, heavy continuous work is a stress that can result in anestrus.

Transportation stress in ewes⁶ and in gilts⁹ induced follicular growth and ovulation in a large number of animals within 4 to 6 days. This phenomena was not reproduced with ACTH injections but severe stress did cause cystic corpora lutea in the ewes. Estrus signs failed to occur in some ewes due to the absence of a regressing corpus luteum with the presence of some progesterone. The author has observed a similar reaction in some transported mares and cows.

Systemic diseases—Severe chronic wasting diseases, such as Johne's disease, tuberculosis, mange, actinomycosis of the jaw, severe parasitisms, and other diseases cause a severe negative energy balance, debility, emaciation and cessation of the estrous cycle.

Pathology of the uterus or cervix is a frequent cause for irregularities of the estrous cycle. In cattle such conditions as pyometra, fetal maceration, mummification of the fetus, and rarely mucometra may cause failure of estrum, and a persistence of the corpus luteum, with a cessation of estrual cycles. A similar effect may be produced experimentally by hysterectomies in cows, swine, does and ewes.²⁷ Early death of the embryo within 20 to 60 days after conception may cause symptoms of apparent failure of the estrual cycle.

Endocrine disturbances often affect the estrous cycle. Cystic ovaries in cattle are frequently a cause for cessation of the estrous cycle. Nymphomania or cystic ovaries in animals are also characterized by irregularities in the estrous cycle and by frequent or continuous estrum. Following calving, ovulations are often associated with a "silent" estrum. This is also observed in ewes and does at the outset of the breeding season and in heifers reaching puberty. It is believed that some of these "silent" estrums are due to an imbalance of estrogens and progesterone with the latter often lacking.^{17b} Short estrous cycles in the cow, long or irregular periods of estrum or lack of estrum, or long diestrous periods in the mare^{3,5,8} are probably of endocrine origin, but the causes for these abnormal long estrous cycles are not fully understood. A long estrous cycle of 25 days was produced in cows infused with an iodine solution on day 15 of the cycle.^{22,23} This was probably due to a lack of prostaglandin caused by damage to the endometrium. Short estrous cycles of 8 to 14 days in cattle have been produced experimentally by infusing the uterus with bacterial contaminants or viral agents such as IBR-IPV at the time of service, infusing the uterus with irritating iodine compounds about the third to sixth day after estrus, injecting large doses of oxytocin from day 2 to day 7 of the cycle, or surgically implanting a foreign object into the horn corresponding to the ovary containing the corpus luteum about the second or third day of the cycle. It is believed that these treatments affect the luteolytic mechanism especially by their stimulation of the production of prostaglandin by the uterine endometrium and possibly by inhibiting the release of L.H. and failure to grow and maintain the corpus luteum.^{15,19,22,23} Large doses of L.H. given during the middle and last week of the estrous cycle may prolong the corpus luteum and the cycle (See Chapter XIII, Infertility in Cattle). In rare cases pituitary, ovarian, and adrenal tumors and their production or inhibition of secretion

of certain hormones may cause marked changes in the estrous cycle.

Miscellaneous causes for irregularities in the estrous cycle include the individual variations between animals in each species. The individual variations are usually minor. However, Brahman and Zebu cattle may have very short estrous periods of only 3 to 6 hours. Copulation usually occurs at night. Pregnancy causes a prompt physiologic cessation of the estrous cycles. The presence of the ram, stallion, buck or boar hastens the onset of estrum when the male is placed with the females late in the anestrus season. This stimulating effect on the release of gonadotropic hormone is probably mediated by visual, auditory and olfactory stimuli to the hypothalamus.^{3,5,4,7}

Thus it can be seen that although the reproductive cycles of domestic animals are primarily under endocrine control they are greatly influenced by the external environment which acts through the central nervous system and the hypothalamus to initiate and regulate the release of tropic hormones from the adenohypophysis.^{3,5,4,8,1,20}

Coition or Copulation

Coitus or the act of copulation, includes the insertion of the erect penis into the vagina, intromission, and the subsequent ejaculation of semen. This takes place only during estrum in the domestic animals. An exception to this occurs in certain barren mares early in the breeding season that exhibit a prolonged period of acceptance punctuated occasionally by true estrum and ovulation. During coitus semen is ejaculated into the vagina and onto the external os of the cervix in the cow, ewe, doe and woman. In the sow most of the semen usually is ejaculated into the uterus since the long narrow penis of the boar enters and "locks" into the cervix.^{6b} During coitus in the bitch, vaginal and uterine contraction waves aid the intrauterine deposition of semen.³ In the mare the penis may be forced against the relaxed dilated cervix and some semen might be ejaculated into the cervix or uterus. At the time of coitus in the mare there is a negative uterine pressure capable of drawing about 80 ml. of fluid into the uterus through the relaxed cervix.⁵ This negative uterine pressure is observed clinically when examining infected, "windsucking" mares especially at the time of estrum. The insertion of the speculum causes a sudden ballooning of the vagina and sometimes the uterus. Bubbles of mucopurulent material may be seen being drawn into the cervix. At the time of intromission the mare can be observed to take a deep inspiration and draw up her abdomen to produce this negative pressure. Us-

ally after an equine service at which time 50 to 100 ml. or more of semen is ejaculated, only 10 or 15 ml. can be recovered from the vagina. This fact is of importance in explaining the cause for infertility in "windsucking" infected mares.⁵ Examining the vagina with a speculum just before service is not advised as this act causes ballooning of the genital tract and prevents the negative pressure normally produced at coitus by the penis sealing the vulva, from drawing the semen into the uterus. More work is necessary on this interesting observation. In the ram the processus urethrae does not enter the external os of the cervix of the ewe during coitus but is responsible for forcibly spraying semen over the cervix and cranial portion of the vagina.⁴

The duration of coitus in cattle and sheep is only a few seconds. In horses copulation is longer, lasting 10 to 30 seconds. In swine copulation takes 3 to 8 minutes with an average of about 5 to 7 minutes. In the dog coitus takes 15 to 30 minutes; the bulbus glandis enlarges slowly, until it is large enough to dilate the caudal portion of the vagina. The sphincter muscles of the vestibule and vulva then contract and the male is unable to withdraw the penis until the bulbus glandis is reduced in size. The male dog usually dismounts and faces away from the bitch during the latter part of copulation.³ In the cat coitus lasts 2 to 5 minutes. (See Chapter XVIII, Infertility in Male Animals.)

It is rather interesting that the structure of the penis is somewhat related to the duration of foreplay and coitus.^{2,2} In ruminants with a fibroelastic type of penis with small vascular sinuses, foreplay and coitus are very brief and the amount of semen ejaculated is small. In animals such as dogs, horses and primates the penis is characterized by extensive vascular sinuses and foreplay and coitus are of moderate to long duration. The exception to this observation is the boar that has a fibroelastic type of penis. The large amount of semen ejaculated in the boar may be a factor causing the prolonged period of coitus in this species. The dog and stallion also have fairly long copulatory periods and they also ejaculate relatively large quantities of semen.

The dangers of coitus to the female animal include the possibility of young, small heifers and fillies or even older females being injured by large or overweight males. These injuries may include fracture of the pelvis, spine, or limbs; dislocation of the hips; muscle or tendon sprains; or injuries to the limbs, udder, or teats. These injuries may be avoided by using smaller males, a breeding rack, or artificial insemination. In both the mare and cow the vagina is shorter than the length of the male's penis, but at the time of coitus the vagina stretches. In spite of this, occasional lacerations and trauma may be produced and

cause swelling, hemorrhage, discharge, and straining following coitus. In rare instances the penis of a bull or stallion may actually rupture the vagina of the female and cause a perivaginal inflammation or abscess with signs resembling acute traumatic reticulitis. Fatal peritonitis may rarely be observed especially when heifers are bred on pasture by a mature bull or large vigorous stallions are bred to small mares. Vaginal and hymenal lacerations with bleeding after service by a stallion occur more commonly during the peak of the breeding season because more mares are bred; the stallions are more experienced and require greater stimulation for ejaculation because of frequent services so thrust deeper with more vigor.

Occasional cases of vaginal rupture and penetration of the peritoneal cavity in the heifer and mare may not result in death, especially if the damage is diagnosed promptly. Treatment consists of stopping further services for a month or more and providing stall rest and tranquilization if signs of colic or discomfort is present. The mare should be given antibiotics and tetanus antitoxin. If signs of shock develop, cortisone and possibly intravenous fluids should be administered. If the mare has pneumovagina the vulva should be promptly sutured.^{6a}

When large stallions are bred to small mares, or when a vigorous stallion with a large penis is bred to average-sized mares, a stallion roll, or if this is not available a double roll of cotton, may be placed against the stallion's abdomen in front of the sheath to prevent too-deep penetration of the penis. In mares with a small vulva it may be necessary to lubricate the vulva to facilitate insertion of the penis. Vaseline or the ordinary water-soluble, neutral, tragacanth gum lubricating jellies are satisfactory. These lubricants should not contain antiseptics. Occasionally feces and other dirt particles are introduced into the vulva and vagina at the time of service and cause irritation and infection.

In a mare with a tipped or horizontal vulva, occasionally the erect penis of the stallion may slide over the vulva and enter the rectum, causing a rupture of the rectal mucosa or the rectal wall. This is called "false entry" and may produce a rapidly fatal peritonitis or a pelvic diverticulum that fills with feces and causes severe straining. This is favored in mares with a vulva that has been sutured by the Caslick technique and not opened sufficiently prior to service. A rectal examination immediately prior to service should not be performed as it stretches the sphincter muscles of the anus of the mare permitting the penis to readily enter the rectum. False entry may also occur in the sow, ewe, doe and cow but apparently it causes little harm in these species. In the

mare if the diverticulum is in the pelvic region caudal to the peritoneum, gentle, regular enemas of physiologic saline or antiseptic solution should be given to keep the diverticulum free of feces until healing takes place. Antibiotics and tetanus antitoxin parenterally are indicated. False entry can be prevented by proper handling of the stallion at the time of service to make certain by manual direction, that the penis enters the vulva.

Occasionally the withers of the mare may be lacerated by the teeth of a stallion or jack at the time of coitus. This can be prevented by muzzling the stallion or by placing a heavy pad over the withers of the mare. Many horsemen believe the stallion has given a "poor service" when he dismounts and the penis on being withdrawn brings with it an ounce or more of semen. Holding the stallion on the mare a little longer allows the size of the glans penis to be reduced and less semen withdrawn. This condition would be more likely to occur if the genital tract was ballooned with air before service, so that the semen was not drawn into the uterus but remained in the vagina. There is no proof that these occasional so-called "poor services" fail to result in conception.

Rarely a mare or cow may have a stenosis of the vagina due to a previous injury or to a hereditary defect of the vulva or vagina, such as "white heifer disease" with an imperforate hymen. In these animals coitus usually results in vaginal or vulvar lacerations and straining. The author has observed two gilts and a sow that died a few days to a week after natural service with severe peritonitis caused by the boar's penis entering the urethra and bladder and passing into a ureter where it caused a rupture about 2 to 3 inches cranial to the bladder. All of these females had cystitis with signs of straining, bloody urine, a swollen vulva, depression and anorexia shortly after an apparent normal copulation. The author has observed and others^{2b} reported cystitis and pyelonephritis in a heifer and a gilt following AI when the semen had been introduced into the bladder. The heifer had a segmental aplasia of the vagina.

Sodomy or carnal intercourse between man and the lower animals is of little importance to the veterinarian, since ordinarily this does not result in injury or disease to the larger animals. In small female animals such perversion may result in injury to the animal's genital canal.

Sadism or sexual perversion in some humans, usually male, may cause them to injure or mutilate, with sharp or solid objects such as broom handles and pointed sticks, the genital organs of animals especially the vagina or rectum of female animals such as mares, cows, goats or sows. Whenever the veterinarian is confronted with a case of injury to the genital organs or rectum of an animal he should attempt to determine the cause, keeping

this possibility in mind, especially if several similar injuries are diagnosed. These injuries are most often perpetrated when the animal is in estrum. Injuries of this type are rarely produced by coitus or by accident but must be caused by some person, usually of low or abnormal mentality, who has access to the animals when no one else is present.⁷

Ovogenesis or Oogenesis

The ovary, besides secreting the necessary gonadal hormones, produces ova. Oocytes are developed similarly in all domestic animals.^{3,5,6,8} Early in the first weeks of embryonal development the primitive large germ cells called primordial germ cells can be identified in the caudal extraembryonal entoblast or yolk sac.⁹ These primordial germ cells migrate by ameboid movement from the yolk sac across the dorsal mesentery to the genital ridges.^{1,2} This migration occurs in porcine and bovine embryos about 24 and 35 days of gestation, respectively.⁴ In a few more days the gonadal sex can be distinguished by the formation of the superficial tunica albuginea and the central location of the germinal cells, spermatogonia, in the primitive testes and the peripheral location of the oogonia in the primitive ovary.⁹ These oogonia multiply by mitosis after sexual differentiation and enter the prophase of the first meiotic divisions when they are called oocytes. The number of oocytes produced may be determined by the level or amount of FSH in the embryo.⁹ Oogenesis is the transformation of oogonia into oocytes. Oogenesis is completed before or shortly after birth in all domestic mammals.^{3,10,14} Sexual differentiation occurs at 30 days of gestation in the feline and porcine embryos, 35 days in the ovine embryo and 45 days in the bovine embryo.⁹ The period of oogonial mitoses, the end of which signifies the end of the major portion of the period of oogenesis, are 32 days of gestation to 37 days after birth in cats, 30 days of gestation to 7 days after birth in swine, 35 to 90 days of gestation in sheep and 45 to 110 days of gestation in cattle. At the end of this period of oogenesis the oocytes enter the first meiotic prophase where they pass through the leptotene and zygotene stage into the pachytene stage. In this stage the ova are surrounded by a single layer of follicular epithelium and these are called primordial follicles.

Thus at birth all female calves and lambs are born with their full complement of oocytes in primordial or older follicles and these are never replenished but only decrease in number during the life of the animal. Bovine oocytes may rest in this pachytene phase for years if the primordial follicle does not grow.⁶ In most species this

resting stage where the oocyte is in the primordial follicle is the dictyate stage.^{7,8,9,10}

In the late dictyate stage as ovulation time approaches, follicle growth and maturation occur. The ovum itself will grow and triple in size in order to provide nutrition for early divisions of the fertilized ovum (See Table 16).

Three types of follicles present at birth and throughout the life of animals are,^{3,4} primordial follicles in which the oocyte is surrounded by a single layer of follicle cells, growing follicles in which the oocyte is surrounded by two or more layers of follicle cells, and vesicular follicles having antrums or fully-formed vesicles. The numbers of germ cells or oocytes in the ovaries of individual cattle is highly variable ranging from 0 (complete sterility) to 700,000. Of 69 cattle examined from birth to

two years of age about 25 percent had 42,000 (0 to 73,000) germ cells, about 60 percent had 137,000 (76,000 to 218,000) germ cells, and about 15 percent of the cattle had 325,000 (223,000 to 724,000) germ cells.^{3,4} The numbers of primordial follicles in cattle remained fairly stable around 140,000 until about 4 to 6 years of age and then declined rapidly thereafter to 25,000 at 10 to 14 years and to near zero at 20 years of age. From 60 days after birth to 10 to 14 years of age the numbers of growing follicles per bovine animal averaged about 150 to 250 and the number of vesicular follicles 25 to 30. In cows over 15 years of age these numbers declined to 70 and 12, respectively. Normal vesicular follicles predominated up to 10 years of age in cows but after that time atretic vesicular follicles were in greater numbers. Two

Table 16. Developmental States in the Maturation of the Ovum*

Chromosome Number		Time Period	
Mitosis	2N	Primordial germ cells	Migrate to gonadal area in bovine embryo
			from 25–35 days of gestation
Meiosis		Oogonia	Multiplication occurs in bovine embryo
			from 45–110+ days of gestation
		Oogonia A	
		Oogonia A (resting)	
		Oogonia B	
		Oocytes, primary	
		Prophase I (1st maturation division)	
		Leptotene stage	
		Zygotene stage	
		Pachytene stage—bovine species	
	4N	Diplotene stage—porcine species	Resting stage
		Dictyate stage—other species	Primordial follicle
			Growing follicle
			Vesicular follicle
		(Diakinesis)	
		Metaphase I	
		Anaphase I	
		Telophase I	Graafian follicle (mature)
			Estrum
	2N	Oocytes, secondary—Ova	1st polar body extruded**
		Prophase II (2nd maturation division)	
		Metaphase II	
		Anaphase II	
		Telophase II	
			2nd polar body extruded
	1N	Union of male and female pronuclei within ovum***	
			Ova transport to uterus
	2N	Zygote	
			Atresia of nonovulating follicles

*After Rajakoski, Henricson and Rajakoski, Kennelly and Foote, Erickson (1965) and Mauleon.

**In bitches and probably mares the 1st polar body is released after ovulation and the 2nd polar body is usually not released unless fertilization occurs. This is probably why the canine ova remain in the oviduct 5 or more days.

***The male and female pronuclei in the rabbit duplicate chromosomes before syngamy thus the fertilized ovum is tetraploid for a very short period until the two-cell stage occurs.¹³

20-year-old cows that had produced 16 and 17 calves, respectively, were considered to be sterile at slaughter with one cow being anestrus and the other showing irregular cycles. The numbers of primordial follicles in these two cows were 100 and 2000, growing follicles 80 and 50 and vesicular follicles 10 and 7. Thus these old cows were approaching the menopausal state that occurs in women. Women had an ovarian oocyte population of 200,000 to 400,000. During the postmenopausal years a complete disappearance of oocytes occur.⁵

Since during the lifetime of a 10-year-old cow producing a calf each year about 30 to 50 ova might be ovulated it is obvious that most oocytes degenerate and die in a process called follicular atresia. Although degeneration of oocytes and follicular atresia may occur in the prenatal period in cattle, germ cell quality in primordial follicles remains high until 6 to 8 months of age and then it declines rapidly thereafter until at 4 years of age and older most oocytes or primordial follicles are in an obvious degenerative state. The process of bovine follicular atresia and oocyte degeneration is a very protracted process extending over a period of years.⁴ Oogonia and oocytes in the first stages of meiotic prophase disappear or degenerate during prenatal and early postnatal periods.^{3,9} Only those oocytes in the pachytene through dictyate stages remain into later life.

Further evidence was presented that following puberty the average bovine female has only approximately 240 oocytes in growing or vesicular follicles upon which she is dependent for the production of fertile ova throughout the rest of her life.⁴ Since the numbers of these growing or vesicular follicles was closely correlated with the total number of primordial follicles there may be a relationship between germ cell numbers and fertility in females. When the ovaries of fertile and infertile 5-year-old cows were compared, the average numbers of primordial, growing, and vesicular follicles present were 119,000 and 18,000; 78 and 35; and 211 and 54, respectively.⁴ In a study on genetic hypoplasia of the ovaries in Swedish Highland cattle normal yearling cattle had an average total of about 50,000 primordial follicles in both ovaries (range 6,000 to 100,000). Heifers with a unilateral partial hypoplasia and unilateral total hypoplasia had 23,000 and 19,000 primordial follicles, respectively, in both ovaries.^{11,12} Of 7 heifers with one ovary completely hypoplastic and the other ovary partially hypoplastic, two heifers had no primordial follicles and five had 100 to 400. In heifers with bilateral total hypoplasia, no primordial follicles were present. Animals with less than 500 primordial follicles did not ovulate. Animals with one hypoplastic ovary had definitely fewer Graafian fol-

licles than normal heifers and were more infertile. In freemartin cattle the gonads have no germ cells.³

Folliculogenesis and Ovulation

Under the influence of the gonadotropic hormones FSH and LH, especially the former, vesicular or Graafian follicles grow and develop. This development occurs in fetal animals, young animals prior to puberty, and even during the pregnancy period. Follicular growth and development culminating in the mature Graafian or vesicular follicle and ovulation occurs only in nonpregnant animals after puberty during a reproductive cycle under the influence of the gonadotropic (FSH-LH) hormone. However horses frequently ovulate during early gestation and diestrus and cows may very rarely do so. The exact mechanisms governing the follicles that mature and ovulate and those that fail to mature and ovulate but regress and become atretic are not understood.

Without the Graafian follicle and the secretion of estrogens and progesterone including some androgens from the granulosa and theca cells under the influence of FSH and LH, signs of estrus would be lacking, ova could not be released and corpora lutea could not form. Growth of the primordial follicles, those where the oocyte is surrounded by a single layer of epithelial cells gives rise to growing or secondary follicles and vesicular follicles or those with antrums called Graafian follicles. In Graafian follicles the oocyte has reached the dictyate stage of development in the cow.^{6,25} By this time the connective tissues around the growing follicle have organized into the theca which consists of an outer zone of stroma cells called the theca externa, and an inner zone of epithelial-like cells called the theca interna which later secretes steroid hormones including estrogens. As growth continues, the antrum forms and enlarges in the epithelial cells around the ovum. The epithelial cells lining this antrum form the membrana granulosa. The fluid in the follicle is called the liquor folliculi. This fluid is believed to be secreted by the granulosa cells. The actively growing Graafian follicle is responsible for its own ovulation by secreting estradiol that causes the LH surge that results in ovulation and the development of the corpus luteum.^{3,6}

In the early stages of the maturation of the ovisac, or follicle, the oocyte is in a mass of epithelial cells, called the discus proligerus, attached to the granulosa layer of cells. The egg and its adjoining granulosa cells are called the cumulus oophorus. Between the cumulus cells and the oocyte proper is the corona radiata, a compact layer

of cells surrounding the zona pellucida, which extends cytoplasmic projections through the zona pellucida to the vitelline membrane to provide nutrients to the oocyte for its maintenance and growth.^{5,27} The cumulus may be located projecting into the follicular fluid anywhere on the circumference of the membrana granulosa.^{5,25} As the follicle approaches maturation and ovulation, the cumulus oophorus either separates from the membrana granulosa and floats free in the follicular fluid or more often it is only tenuously attached. The ascent of the follicles to the surface of the ovary coincides with the appearance of the thecal layers. The theca interna develops a wedge-like cone that precedes the follicle through the ovarian stroma to the surface. In all species of domestic animal, except the mare, ovulation can occur over the entire ovarian surface. In the mare ovulation occurs only in the ovulation fossa or concave ventral medial portion of the ovary that is not covered by a dense tunica albuginea and mesovarium.^{5,14,21,24,29}

Ovulation takes place by a thinning process, usually avascularization and rupture, with slight bleeding, of the outer portion of the follicle wall and peritoneum. The ovum with the enclosing cumulus cells are washed out in the gradually-released gelatinous follicular fluid and are caught by or pass into the fimbriated end and ampulla of the uterine tube, where fertilization takes place.⁸ In the cow, mare and other species the outer thin follicular wall that usually feels tense and firm during proestrus and early estrus becomes more flaccid and soft just prior to ovulation.^{5,6} In rare instances the ovum and its cumulus cells may be caught and retained in the collapsing walls of the Graafian follicle at the time of rupture. This may be a rare cause for failure of fertilization.

In domestic animals a circumscribed avascular area appears on the apex of the follicle that projects above the surface of the ovary.^{6,3,4} This thins out until a fine transparent membrane bulges above the surface. This is the basement membrane separating the granulosa and thecal layers of the follicle. This breaks and the follicular contents ooze from the follicle. Collapse of the follicle walls doesn't occur until after the cumulus has passed through the small stigma in the surface of the follicle. Ovulation may require a few seconds to several minutes or longer depending on the size of the stigma and the location of the cumulus in the follicle.

Intrafollicular pressure is not the cause for ovulation.^{6,4} The stigma is small and nearly round or oval. There is no sign of tearing of the follicle wall. As noted above just prior to ovulation the follicle becomes more flaccid and less tonic. Observed ovulations are not violent eruptions. Where the intrafollicular pressures have been measured there has been no increase in pressure

prior to ovulation. Recent work presented evidence to indicate that ovulation was probably brought about by the release of LH that releases histamine and possibly prostaglandin⁶ causing ovarian hyperemia. This hyperemia may stimulate the release of proteolytic enzymes, such as collagenase into the follicular fluid which may be responsible for the separation of the cumulus from the side of the follicle. Thus the proteolytic enzymes weaken the wall of the follicle and the stigma or avascular area develops and ovulation occurs at the superficial projecting area where the wall is not supported by the ovarian stroma.^{15,23}

After the follicle ruptures and the ovum is released a slight amount of bleeding may occur into the follicle. This is then called the corpus hemorrhagicum in the cow, ewe and sow and other species. In the mare a large blood clot, which can be palpated per rectum, and may feel like a follicle, fills the large lumen of the follicle. This bleeding occurs through the follicle walls and not at the site of rupture of the follicle. In the cow fibrin "tags" may develop on the ovary or fine adhesions between the ovary and the fimbria may occur following ovulation. This has no effect on fertility. It is possible that the enzyme reaction that weakens the follicle wall to produce ovulation acts for a longer period of time in the mare and therefore a greater amount of bleeding occurs through the follicle wall after ovulation.

Ovulation is largely under endocrine control. Under the stimulus of FSH from the anterior pituitary a number of vesicular follicles begin developing. As these follicles develop, an increasing amount of estradiol is produced by the theca interna and is absorbed into the circulation of the body as well as being present in the follicular fluid. In the body estradiol produces the typical changes in the tubular portion of the reproductive tract seen in proestrus and estrus. It also produces the characteristic symptoms and manifestations of estrus or heat by its action on the central nervous system. Except for the follicles that are to mature, usually only one in uniparous animals and a moderate number in the multiparous animals, there is a sudden wave of atresia that strikes many different size follicles a short time, about 12 to 24 hours or possibly more, before ovulation of the mature follicle. Atresia of the small Graafian follicles begins in the oocyte while in medium and large Graafian follicles atresia begins with degenerative changes in the granulosa and theca interna with the changes in the oocyte developing slightly later.^{6,25} Obliterative atresia occurs in small and medium-sized follicles but in large follicles cystic atresia occurs in which the antrum and follicle fluid are reduced only after complete degeneration of the follicle wall with fibrotic changes in the theca. Follicular atresia can occur

at any stage of growth, and degeneration of the oocyte may start at any stage of atresia.¹⁶ Cystic atresia may occasionally be associated with a degree of luteinization of the cystic follicle.

The cause for the atresia of the "second rank" follicles and the mechanism controlling the number of follicles allowed to mature and ovulate are not known.

Progesterone produced in the Graafian follicle before ovulation may play an important role in cattle in the release of LH and ovulation.^{6-9,11} More work is required in order to elucidate the nature of the exact mechanism of ovulation in animals. Release of LH by the anterior pituitary is necessary for and causes ovulation of the mature Graafian follicle. A large amount of LH is released from the bovine anterior pituitary gland usually within 1 to 5 hours after the onset of estrus by the stimulus of a rising estradiol blood level produced by the maturing follicle.^{5,11,13,26}

The corpus luteum which was already developing from the granulosa cells lining the Graafian follicle at the time of ovulation grows very rapidly following ovulation. The production of progesterone by the corpus luteum then suppresses LH and FSH production. If fertilization and pregnancy take place, the corpus luteum is maintained by the secretion of luteotropic hormone or LH from the anterior pituitary gland and the lack of release of prostaglandin from the endometrium caused by the influence of the conceptus. If pregnancy does not occur, then the corpus luteum degenerates and, with the decline in the production of progesterone late in the estrous cycle FSH and LH are again produced and a new wave of follicles begins to grow followed by the onset of proestrus. The approximate minimum time required for the development of the follicles and ovulation in domestic animals is 3 to 4 days, as revealed by work on sheep, and the manual removal of the corpus luteum in the cow.

In the cow a wave of follicular growth with an accumulation of small Graafian follicles, less than 5 mm in diameter occurred during the third and fourth days of the cycle resulting in a large follicle 9 to 18 mm in diameter at the 13th day. A second-wave of follicular growth occurred between the 12th to 14th day with the production of small follicles 5 to 8 mm in size resulting in a single large follicle, 12 to 16 mm, at 16 days that usually ovulates 4 or 5 days later.²⁵ A wave of atresia follows each growth wave leaving in most cows only one large follicle. Thus it apparently took 7 to 9 days from early follicle growth to ovulation in the cow. This diphasic growth wave of follicles has not been reported in other domestic animals.

Recent studies have shown a continuous growth and atresia of large follicles during the estrous cycle in the

cow with an increased rate of atresia, growth and replacement from day 13 to ovulation, especially after day 18.^{5,12,19,28,30} Small follicles decreased from day 3 to 18 and medium sized follicles were most numerous day 13 just after blood estrogen levels rose at mid cycle. These studies did not support the previous two-wave theory of Rajakoski.²⁵ The corpus luteum has an inhibitory action on large follicles on days 8 to 13 even though medium-sized follicles increased. Apparently the largest active follicle in unipara exerts an inhibiting intraovarian effect on smaller follicles.¹⁹ The ovulatory follicle in the cow varies from 10 to 20 mm. in diameter and secretes large amounts of estradiol at the time of onset of behavioral estrus that promotes the LH surge.²⁸ The latter hormone acting on the LH receptors in the granulosa cells induces ovulation of the follicle.

Even though nearly all the reproductive function can occur without nervous innervation of the lower portion of the body, there is definite evidence that ovulation, as well as other phases of the reproductive cycle, are influenced by the nervous system in the intact animal. Heifers, when bred by a vasectomized bull, ovulated an average of 7.7 hours after the end of estrus as compared to 9.9 hours when not bred.¹⁸ The ovulation of heifers was delayed 24 to 66 hours by the administration of massive doses of atropine at the onset of estrus; but when chorionic gonadotropin, or LH was administered shortly after the atropine, ovulation occurred about 10 hours earlier than normal.⁷ This indicated that atropine prevented the normal release of LH from the pituitary. The administration of gonadotropic hormone during early estrus shortened to 1.25 hours the normal time of 10.5 to 12.25 hours from the end of estrus to ovulation.¹⁷ Progesterone given in 5 to 15 mg doses intramuscularly at the onset of estrus reduced the average length of estrus 3.6 hours, the average time from the end of estrus to ovulation 5.4 hours, and the average time from the onset of estrus to ovulation by 9 hours.⁸ Atropine blocked the effect of progesterone and this blocking action took place in the hypothalamus.¹¹ The LH release mechanism is stimulated by the action of estrogen, and in certain species other external factors such as coitus in the queen, affecting the hypothalamus.

Ovulation is spontaneous in all animals except the rabbit, cat, and ferret. In these latter species one or repeated mountings or intromissions may be required to release LH from the pituitary and cause ovulation. Ovulation in these species may be caused by stimuli, such as gently manipulating a glass rod in the vagina simulating coitus or by the injection of luteinizing hormone. Ovulation usually occurs at a fairly constant time following the stimulus of coitus or the injection of LH at estrus. In the

rabbit it occurs about 10.5 hours later, and in the cat about 27 hours later. This stimulus in the rabbit is apparently emotional and can be produced by the excitement of being mounted by another doe. It can also be produced by coitus when the vagina and vulva are anesthetized.²

When 25 I.U. of LH was injected intravenously into isolated mature female rabbits, 50 percent of them ovulated between 10-1/2 and 10-3/4 hours later. This therapy can be given to queens to terminate estrus. These are other examples of the way in which peripheral and central nervous stimuli affect ovulation.

With the exception of the cow, ovulation usually occurs before the end of estrus in all domestic animals that ovulate spontaneously. The cow, due to its low threshold for estrogen, remains in estrus only a short period and then an "estrous block" of central nervous origin develops and the cow goes out of estrus even though additional amounts of estradiol are being produced.¹ The approximate time of ovulation for the various domestic animals is as follows.^{2,3,2,9,8,11}

Cow and ewe—about 24 to 30 hours after the onset of estrus. In the cow this is 10 to 14 hours after the end of estrus.

Sow—about 35 to 45 hours after the onset of estrus.

Mare—about 4 to 6 days after the onset of estrus.

Bitch—24 to 48 hours after the onset of estrus.

Queen—24 to 30 hours after onset of estrus and coitus.

The ovum of the bitch and probably the mare don't extrude the first polar body for several days after ovulation at which time fertilization can occur.^{3,6,8}

Superovulation—Discovery of the gonadotropic hormones, and interest and research in embryo transfer have resulted in experiments on various means of inducing superovulation, or the release of numerous ova from the ovaries of uniparous animals. (See Chapter 20.) This can be produced during late metestrus, diestrus, and early proestrus by daily subcutaneous injections of FSH for 3 to 6 days, followed by an intravenous injection of LH, or, if timed properly so that the last FSH injection comes just before estrus, the cow may ovulate the numerous artificially produced follicles by means of its own secretion of LH.^{6,2,5a,5b} (See Chapter XX.) Superovulation can be produced in cattle by injecting 2,500 to 3,000 I.U. of PMSG intramuscularly on the 16th day of the cycle or when the corpus luteum is manually removed. Five days later 2,000 I.U. HCG may be given intravenously to promote ovulation although it is not necessary as the female's own LH causes ovulation. In sheep and goats 1,000 to 1,500 I.U. PMSG injected on the 12th day and 16th day of the cycle, respectively, will induce

superovulation in these species. In sows and mares FSH injections to cause superovulation is not yet satisfactory or practical. PMSG is of no value for superovulation in mares and presently is not available in the U.S. In cattle about 15 percent of the superovulated ova were morphologically abnormal.

By using prostaglandin preparations superovulation to obtain embryos for transfer is facilitated. Presently PMSG or more commonly a purified FSH gonadotropic product is injected into the donor cow on day 8 to 12 of the estrous cycle. The gonadotropic hormone (FSH) is given twice daily at gradually reducing doses for 5 days.² On the third day after the initial injection of either PMSG or FSH, a luteolysing dose of prostaglandin is administered with estrus occurring several days later. In cows the desired number of embryos produced is about 8 to 10. There are great sources of variation in the response of cows to gonadotropins and the number of ova or embryos produced. These variations have been related to the variable potencies of the gonadotropic hormones employed and the different breeds and ages of cattle used as donors. Further study is indicated.^{1,2}

Because numerous corpora lutea form following superovulation the bovine ovary may be five to ten times normal size. Thus it is recommended not to inject FSH into animals 4 to 5 days prior to estrus if superovulation is to be avoided. A cow given PMSG, "Gonadin" was bred and conceived 6 days later but aborted sextuplets at 6 months of gestation.²⁰ After repeated injections of gonadotropic hormones cows may become refractory to them unless a proper "rest" period is provided. Since antihormones are produced when impure products are used, repeated injections of the proteinaceous gonadotropic hormones may result in fewer ova being ovulated.

Ova (Embryo) and Sperm Transport and Fertilization

Ova transport—As ovulation approaches there is a marked increase in the tonicity, edema and motility of the fimbriae of the uterine tubes in domestic animals; the fimbriae nearly clasp the ovary in order to receive the egg. These effects are under the endocrine control of estrogen during the estrous period. Following ovulation, the cumulus oophorus which was liberated from the mature Graafian follicle is transported from the surface of the ovary into the uterine tube. This transfer is effected by the direct action of the cilia of the fimbria and infundibulum on the cumulus as well as the currents of fluid created by the beating cilia flowing toward the ostium of the uterine tube. Essential to these immediate transport mechanisms are the contractions of the smooth

muscle of the mesovarium and regular contractions that change the position of the ovary with respect to the infundibulum and fimbria.^{3,6,9,22,25}

The rate of transport of the ova through the ampullary portion of the oviduct to the area of the ampullary-isthmic junction is quite rapid and is probably accomplished in a relative few minutes, 8 to 30.^{3,6,8} This transport is effected by peristaltic and antiperistaltic muscular contractions of the smooth muscle in the ampulla together with ciliary activity under the hormonal control of estrogens. The cilia in the rabbit uterine tube beat at a rate of 1500 per minute. The beat of the cilia towards the uterus creates currents in the tubal fluid and the contractions of the uterine tube keeps the ovum in constant motion which aids in egg and sperm contact and fertilization.^{6,22,25} Sperm penetration of the ovum and fertilization which requires several hours, occurs in the ampulla of the uterine tube. The physiological significance of the oviduct fluid which is secreted in greatest amounts during estrus is not well understood.²⁵ Most of this fluid passes into the peritoneal cavity. Adhesions and obstruction or ligation of the distal or fimbriated portions of the bovine uterine tube causes hydrosalpinx. Some fluid may pass through the isthmus into the uterus.

The ova or eggs of domestic animals at the time of ovulation are one of the largest cells in the body and vary from 120 to 185 microns or 0.12 to 0.185 mm in diameter not including the zona pellucida.^{6,1,23} In ungulates the ovum contains very little glycogen but large amounts of lipid material; whereas in rodents the reverse is true. These materials are necessary for energy production to produce protein biosynthesis in the ovum. Certain ova may be defective and have obvious structural abnormalities including: small or giant ova, oval or flattened ova, ova with a ruptured zona pellucida, ova with large polar bodies or vacuoles within the vitellus, ova with an abnormal cytoplasm, abnormal-shaped ova, atypical 2-blastomere ova and etc.²³ These abnormal or degenerated eggs may be due to improper maturation of the oocyte, genetic or environmental factors or failure of polar body extrusion. The incidence of abnormal ova varies between the breeds and strains and is greatest in older females.^{6,23}

The cumulus and corona cells around the zona pellucida of the ovum in most domestic animals only persist for a few hours or less after ovulation and fall away in the oviduct. In the bitch and queen the corona cells may persist for several days. The protoplasmic projections from these cells into the zona pellucida are withdrawn soon after ovulation due to contact with fibrinolytic enzymes in the oviduct fluid. The cumulus and corona cells die and separate from the ovum aided by the ciliary and

muscular activity of the oviduct. Inside the zona pellucida is the vitelline membrane or vitellus which is similar to the plasma membrane of somatic cells. The zona pellucida is a homogeneous semipermeable structure surrounding the ovum composed of conjugated protein capable of being dissolved by proteolytic enzymes such as trypsin and chymotrypsin. After fertilization the vitellus shrinks and a perivitelline space is formed between the zona pellucida and the vitelline membrane into which the polar bodies are extruded.

Most ova of domestic animals have ovulated when the second maturation division has reached metaphase and the first polar body has been extruded. In the bitch and probably the horse, ova are ovulated as a primary oocyte and mature in the oviduct. The fertile life of ovulated ova in domestic animals is relatively short, 6 to 24 hours or less except in the bitch where they may remain fertile in the uterine tube for 4 or more days due to their delayed maturity.^{3,6,8} In cattle inseminated 2 to 4 hours after ovulation both the conception rate and the percentage of normal embryos at 35 days were 75 percent.¹¹ When insemination took place 6 to 12 hours after ovulation the conception rate was 60 to 75 percent but only 30 percent of the embryos were normal at 35 days. Insemination after 12 hours following ovulation resulted in conception rates that were very low, and normal embryos were unusual. A high rate of fertilization in cows inseminated at 13 hours post-ovulation in cattle but no fertilization at 16 to 22 hours postovulation was reported.³³ The loss of fertility or viability is not rapid or sudden and aging eggs may be fertilized normally but produce embryos that die early in gestation. With further loss of viability of the ovum, fertilization may be abnormal or fail to occur. Under usual conditions of estrus and natural service in situations where a male is present with the females, spermatozoa will reach the site of fertilization in the oviduct before ovulation and the arrival of the ova. Under conditions of artificial insemination this orderly sequence of events may be altered and infertility result. Fertilization of "old" eggs in swine is associated with polyspermy and abnormal development.²⁹

In domestic animals the eggs or ova remain in the oviduct in the ampullary-isthmic area for 3 to 4 days before passing rapidly through the isthmus and the uterotubal junction into the uterus. In the sow the ova may pass into the uterus in 1-1/2 to 3 days possibly associated with multiple ovulation.³ After rapid transfer to the ampullary-isthmic junction, swine eggs remain there for about 30 to 45 hours and enter the uterus 30 to 60 hours after ovulation.⁴⁰ Ovine ova remain in the ampullary-isthmic junction for 50 to 60 hours following ovulation due to the strong antiperistaltic contractions in the isthmus.⁶ In

most domestic animals fertilized ova require 3 to 5 days to pass through the uterine tube into the uterus; but may require 6 to 8 days in the dog, 5 to 9 days in the cat, possibly 6 days in the mare² and 2 to 3 days in the sow.^{1,3,6,8} An accelerated rate of uterine tubal transport of ova has been reported in superovulation in the cow possibly due to elevated steroid levels.¹⁶ The normal transport of ova through the uterine tube can be severely disturbed by injections of estrogen, progesterone or other drugs and anesthetics. The stage of the estrous cycle, the species of animal and the dose levels of the above agents all produce varying effects on the isthmus and the rate of ova transfer to the uterus.²⁵ Depending upon the dose of estrogen and the species injected some ova may be trapped or blocked in the ampullary-isthmic portion of the uterine tube, "tubal locking"; while in others the ova are rapidly passed into the uterus and are expelled through the cervix into the vagina.²¹ The failure to demonstrate "tubal locking" in a recent experiment may have been due to the very low dose of estradiol injected.¹⁶ These effects appear to be due to the reaction of the isthmic portion of the uterine tube to the injected hormone or drug. It has been suggested that edema in the isthmic area might play a role in tubal regulation of the time of transport, but muscular effects by the gonadal hormones seem more logical from the evidence.⁸ Under ordinary conditions the fertilized ovum or developing zygote remains in the uterine tube until the corpus luteum is formed and the endometrium is under the influence of progesterone so a proper environment and nutrition is available upon entering the uterus. If the egg is not fertilized it fragments into many irregular cytoplasmic segments and disintegrates in the uterus under the influence of phagocytosis. In the mare unfertilized ova may be retained in the uterine tube for weeks or possibly months. This trapping phenomenon has been reviewed² but no satisfactory explanation has been proposed other than the possibility that the fertilized ova by its "hormonal" secretions controls its passage through the uterine tubes.

Sperm transport in the female—In the cow, ewe, bitch and queen the ejaculate at coitus is forcibly sprayed over the cervix and anterior vagina forming a "seminal pool" in the cranial portion of the vagina. In the bitch the large ejaculate, 7 to 20 ml., is carried into the uterus through the relaxed cervix by the muscular activity of the genital tract. In the mare and sow, as described earlier, the semen at coitus is largely placed into the uterus. There is no evidence that seminal fluid passes from the vagina into the uterus in the cow, sheep, queen, doe or man.³⁹

After ejaculation the spermatozoa in the seminal plasma migrate or diffuse from the plasma into the mucus of the

female genital tract where they may be protected, nourished and transported. In the cow as much as 150 ml. or more of cervical mucus may be obtained at estrum. Bovine cervical mucus contains mucoids (amino acids, sugar and sialic acid), glycogen, protein, enzymes, globulins, salt, urea and very small amounts of glucose. Vaginal and cervical mucus in the other domestic animals under the influence of estrogens also changes from a tough tenacious consistency in diestrus or anestrus to a more liquid, viscid, stringy mucus during proestrus and estrum. This permits and favors sperm cell migration. The velocity of sperm cells in bovine cervical mucus at estrum is 56 microns per second, (3 mm./minute) versus 132 microns per second in saline.⁴² The "fern test" of cervical mucus is positive when mucus from the cow or other animals in estrum is smeared on a slide and allowed to dry producing a fern-like aborization due to the high NaCl and water content of the mucus at this stage of the cycle. No specific substance harmful to spermatozoa has been recovered from normal cervical mucus. Leucocytic phagocytosis, bacterial endotoxins, and abnormal pH may play a role in preventing the penetration of sperm cells through cervical mucus. "Hostile" cervical mucus is a catchy term loosely used to describe certain conditions affecting the cervical mucus in women.

The passage or transport of spermatozoa from the vagina through the cervix and uterus and into the uterine tube is very rapid, less than 15 minutes, in all domestic animals and man. Sperm cells in the bitch are at the uterine entrance of the uterine tubes 25 seconds after ejaculation.² Spermatozoa have been found throughout the bitch's genital tract within 20 minutes after the onset of copulation. This transport time was 8 minutes in the ewe.³⁶ It was demonstrated that in the cow spermatozoa were transported from the cervix to the ovarian ends of the uterine tubes in less than 2 to 4 minutes.^{45,46} This occurred whether the spermatozoa were living or dead and followed either natural or artificial insemination. The interval from ejaculation to the presence of spermatozoa in the uterine tubes was reported to be somewhat longer in species other than the cow, one-half to several hours.³ Spermatozoa could also gain entrance to the uterine tubes in cows and sows during the luteal phase of the cycle.²⁰

Movement of the spermatozoa in the uterine lumen is due to strong contractions of the uterine wall augmented by the release of oxytocin at coitus or artificial insemination.⁴⁶ Fright and/or excitement might release epinephrine and interfere or inhibit temporarily the uterine contractions. There is no evidence that epinephrine release at coitus or soon after affects fertility. Prostaglandin, a substance from the seminal vesicles present in sheep, goats, possibly other animals, and human semen

is an oxytocic agent that can also stimulate the smooth muscle of the genital tract. Since the vaginal mucous membrane is permeable to prostaglandin it may also play a role in spermatozoan transport.⁴² The spermatozoa are thus transported largely in a fluid medium or mucus by capillary action in the cervix and by ciliary activity and contractions of the walls of the genital tract. The sperm cell's contribution to this transport up the female tract is a small one because of the relatively slow rate of movement for the long distance to be traversed. However, this motility of the spermatozoa is probably important at the natural barriers of the cervix, the utero-tubal junction, the isthmus of the oviduct and in the initial penetration of the sperm cell into the cumulus. Motility of the sperm cell is essential to fertility. Since dead sperm cells and inert particles will pass through the uterus and into the uterine tube, the motility may be most essential to traverse the cervix and penetrate the cumulus cells or zona.³⁶

Millions to billions of spermatozoa are usually ejaculated into the female genital tract of domestic animals at coitus. In the mare, bitch and sow most of these promptly enter the uterus. In the other species only about 10 or 100 million spermatozoa pass through the cervix into the uterus with more sperm cells being in the base of the horns than in the apex of the horns. Several hundred to less than a thousand spermatozoa gain access to the ampulla of the uterine tube, and only 10 to less than 100 would be in vicinity of the unfertilized ovum. Apparently the uterotubal junction and the isthmus have some controlling role in the numbers of spermatozoa that gain access to the uterine tube. In the rabbit after mating, and just before ovulation, the distribution of spermatozoa in the doe's genital tract were as follows: 20×10^6 sperm cells in the vagina, 12×10^6 in the caudal portions of the uterus, 50×10^4 in the apical portions of the uterus, 4×10^3 in the uterine tubes but only 500 spermatozoa in the ampulla of the uterine tube where the ova were fertilized.¹⁰ In sows the number of spermatozoa in the uterine tube is affected by the volume of semen entering the uterus as well as the concentration or numbers of spermatozoa.⁵ When 1 ml. of fresh or frozen semen containing millions of live spermatozoa was placed in mid-cervix in heifers, 4 hours later 469 and 191 spermatozoa were in the uterine tubes, and 1559 and 733 spermatozoa were in the uterus, respectively.³⁰ Four hours after insemination only 3 percent of the inseminated spermatozoa could be recovered.

A review of the literature, indicates that in mammals only a small proportion of spermatozoa ejaculated at coitus reach the distal end of the uterine tube.³² Some sperm cells may actually enter the peritoneal cavity.²⁵ Apparently natural barriers at the cervix and uterotubal junc-

tion limit the number of spermatozoa going to the site of fertilization. Rabbits inseminated with less than 20,000 to 100,000 spermatozoa per insemination failed to conceive.¹⁵ This number of spermatozoa varied with the extender and the degree of dilution. A 0.6 percent decline in conception rate in cattle with each million decline from 12,000,000 to 4,000,000 spermatozoa inseminated was reported.⁴⁷ Below the latter figure the decline in conception rate was very rapid, about 3.6 percent for each million decline in sperm cell numbers to about 1,500,000. Conception rates, when 12 to 14 million, 6 to 8 million, and 1 to 3 million actively motile bovine spermatozoa were inseminated were 67, 64 and 49 to 53 percent, respectively when based on 60 to 90 day nonreturns.

Thus a minimum number of motile spermatozoa is necessary for fertilization and conception. In sows and probably mares and bitches a minimum volume of ejaculate or artificially inseminated semen is also necessary for optimum conception rates.

In most domestic animals sperm cells can only retain their viability and fertility at a high level for about 24 to 48 hours in the female genital tract. The longest fertile period for spermatozoa in the female tract of most domestic animals is 48 to 72 hours.^{3,5,8} In the mare and the bitch spermatozoa may survive and be fertile for 5 to 6 days. Like aging ova, aging spermatozoa may be capable of fertilizing the ovum but this may result in embryonic deaths.²⁹ The most common result of aging spermatozoa whether they age in liquid semen at 5°C or in the female genital tract is failure of fertilization. The loss of fertilizing capacity of frozen semen, especially in liquid nitrogen, is very slow and gradual and extends over a number of years.

The vagina of the sow and ewe is not a favorable site for sperm cell survival and they lose their motility and die in 6 to 12 hours or less. The cervix with its viscous mucus of estrum is the most favorable site for the survival of spermatozoa in the cow and ewe. Sperm cells live in the cervix for 36 to 48 hours or possibly slightly longer and this site appeared to act as a sperm cell reservoir for spermatozoa in the cow, ewe and doe.^{35,36} Sperm cells retain their motility in the uterus and oviducts for about 24 hours. The uterus is not a highly favorable site for sperm cell survival because the presence of spermatozoa stimulate the invasion of leucocytes and the phagocytosis of spermatozoa. In swine it was shown that by 30 minutes after service the volume of seminal fluid in the uterus was greatly reduced and leucocytes were entering the lumen.³¹ Sperm cell survival in sows appeared to be longest in the mucous folds of the uterotubal junction. Ciliated cells in the apex of the uterine horns of sows were observed. By 8 hours postcoitus the

numbers of leucocytes were greater than the spermatozoa and by 27 hours after service only rarely were spermatozoa found in the sow's uterus. The uterotubal junction was a "sperm reservoir" in the sow.²⁵ The elimination of spermatozoa following their death in the female genital in the other domestic animals is by phagocytosis as in the sow.^{34,35} Possibly a few dead spermatozoa may be expelled through the dilated cervix.

Fertilization of the ovum occurs in the ampulla of the oviduct within one to two hours after ovulation if the spermatozoa are present in the oviduct. By this time the second reduction division of the ovum is in progress except in the bitch and probably the mare in which this division is delayed.⁶ Fertilization involves the penetration of the ovum by the spermatozoon, the activation of the ovum, the formation of the male and female pronuclei and the mingling of the maternal and paternal chromosomes to constitute the genome of the new zygote with a diploid number of chromosomes. A recent study reported evidence for species-specific sperm plasma membrane receptors for the zona pellucida. This sperm-egg interaction further assures their mutual attraction and the process of fertilization.^{3,41}

Capacitation of spermatozoa is the process that spermatozoa of all animals must undergo in the uterus or oviducts before achieving the capacity to fertilize ova. Capacitation time in sheep is 1-1/2 hours. Capacitation time in the other domestic animals is also about 1 to 6 hours.^{3,33} There is evidence that ejaculated bull, stallion and boar semen has a decapacitation factor that is lost in the female genital tract.^{3,6} In rabbits spermatozoa placed in the oviducts 2 hours before or after ovulation failed to result in conception. If they were placed in the oviduct 4 hours before, 6 percent of the ova were fertilized, and 6 hours before ovulation, 78 percent of the ova were fertilized.^{13,14} Spermatozoa can penetrate porcine ova within 3 hours of insemination.²⁷ Capacitation produces a change in the acrosome called the "acrosome reaction" with a release of lytic enzymes such as hyaluronidase. No changes occur in the sperm head proper in the uterus but a functional change in the sperm head may take place when the sperm cell contacts the granulosa cells of the cumulus. Thus capacitation may allow the "acrosomal or vesiculation reaction" to occur to permit the sperm cell to penetrate the granulosa cells and zona pellucida. This enzyme permits the sperm cell to penetrate the cumulus cell mass around the ovum by depolymerizing the hyaluronic acid-protein matrix of the cumulus. The cumulus cells including the corona radiata in most domestic animals break down and separate from the zona pellucida early. In the bitch and queen the corona cells may remain for some period of time. This early breakdown of the cumulus cells is caused by autolytic changes, ac-

tion of the bicarbonate ions in the oviduct, ciliary and muscular activity of the oviduct and hyaluronidase or possibly other enzymes if spermatozoa are present.

Before the sperm cell can penetrate the zona pellucida it loses the acrosome cap and plasma membrane exposing the perforatorium and inner acrosomal membrane which are responsible for the penetration through the zona pellucida.^{3,4,6,7} It is reported that a lytic enzyme such as trypsin together with hyaluronidase may permit the sperm cell to dissolve in oblique "tunnel" through the proteinaceous zona into the perivitelline space.⁴³ When the plasma membrane of sperm head and vitelline membrane are in contact, the two structures unite and the entire sperm cell passes into the cytoplasm of the egg. In certain sterile bulls, boars and dogs, the spermatozoa have defective or knobbed acrosomes. These animals are sterile because their spermatozoa cannot penetrate the ovum. Usually when the sperm cell contacts the vitelline membrane in most domestic species, maturation of the ovum by meiosis is resumed with the expulsion of the second polar body. The cause of this "activation" of the ovum is not known but it proceeds to pronucleus formation.

Two factors are apparently responsible for preventing, except on rare occasions, the penetration of more than one sperm cell into the ovum. The first is the relatively few spermatozoa in the oviduct at the time of fertilization. The second is when the first sperm cell contacts the vitelline membrane a rapid reaction takes place both in the zona pellucida and the vitelline membrane that blocks the further entrance of sperm cells.^{1,2} It is believed that this reaction is brought about by the release of a substance from the vitelline membrane or the cortical granules just beneath this membrane. It is not uncommon when examining fertilized eggs to see many sperm cells on or in the zona pellucida and in certain species in the perivitelline space.

After the male and female pronuclei form, the chromosomes in each pronuclei unite to form the zygote. This union of the two chromosome groups is called syngamy, at the conclusion of which fertilization is complete. The diploid or tetraploid zygote usually immediately divides into two blastomeres and the cleavage of the ovum progresses rapidly in the next few days to the blastula stage.^{44b} The approximate number of days from ovulation to the blastocyst stage of development is 6 in the horse, 7 to 8 in the cow, 6 to 7 in the ewe, 5 to 6 in the sow and 4 to 5 in the queen. The time of entry of the cleaving fertilized ova into the uterus in domestic animals is about 2 to 6 days after ovulation. This is usually shorter in swine and in superovulated cattle,^{1,2} longer in bitches, queens and mares. The passage of the ova through the isthmus of the uterine tube is rapid. The passage of the fertilized cleaving ovum into the uterus and the control

of this passage by the gonadal steroidal hormones acting on the muscular isthmus of the uterine tube has been described previously. Some interesting time relations in regard to fertilization in domestic animals have been reviewed.² Sperm cell penetration of the ovum begins about 3 hours after ovulation in ewes, pronuclei are formed 11 to 39 hours after ovulation in the cow and 3 to 9 hours after ovulation in the ewe. The fertilized egg divides into the two-cell stage about 24 hours after ovulation in the mare and 19 to 24 hours after ovulation in the ewe.

The most common abnormalities of fertilization are polygyny and polyspermy. Polygyny is incomplete maturation of the egg with a failure to expel the second polar body resulting in a triploid zygote. Polyspermy where more than one, usually two, sperm cells enter the egg is also characterized by triploidy or a 3N instead of a normal 2N chromosome complement in the zygote. Aging of the egg increases the incidence of these anomalies. Twenty percent or more of swine zygotes were polyspermic or digynic when the sow was bred more than

Table 17. The Reproductive Cycle of Domestic Animals*

Animal	Onset of Puberty	Average Recommended Age for First Service	Length of Estrous Cycle	Follicle Diameter (mm)	Length of Estrum	Time of Ovulation	Optimum Time for Service	Ovum Transport Time	Advisable Time to Breed After Parturition
Mare	10–24 m. (18 m.)	2–3 yr.	19–23 d. (21 d.)	35–55+	2.0–13 d (7.2±2.9 d) (5.7 d)	1–2 d. before the end of estrus	2–4 d. before end of estrus or the 2nd–3rd d. of estrus	4–6 d.	About 25–35 d. or 2nd estrus; about 9 d. or 1st estrus only if normal in every way
Cow	4–24 m. (6–18 m.)	14–22 m.	18–24 d. (21 d.)	10–20	12–28 h. (18 h.) (Temperate Zone)	10–15 h. after the end of estrus	Just before the middle of estrus to the end of estrus	3–4 d.	60–90 d.
Ewe	4–12 m. (first fall)	12–18 m.	14–20 d. (16.5 d.)	15–19	24–48 h. (30–36 h.)	12–24 h. before the end of estrus	18–24 h. after the onset of estrus	3–4 d.	Usually the following fall
Goat	4–12 m. (first fall)	12–18 m.	15–24 d. (20 d.)		30–60 h. (36–48 h.)	About the last day of estrus	24–36 h. after the onset of estrus	3–4 d.	Usually the following fall
Sow	5–8 m.	8–9 m.	18–24 d. (21 d.)	7–10	1–4 d. (2–3 d.)	30–40 h. after the onset of estrus	12–30 h. after the onset of estrus	2–3 d.	First estrus 4–9 d. after weaning pigs
Dog	6–12 m. (7–10 m.)	12–18 m.	1–3 cycles per year (1.6 cycles per year) aver. every 7 months	6–8	4–12 d. (9 d.)	1–2 d. after the onset of true estrus	2–3 d. after onset of true estrus or 10–14 d. after onset of estrous bleeding	6–8 d.	Usually the first estrus or 3–4 weeks after weaning pups
Cat	6–15 m. (8–10 m.)	12–18 m.	15–21 d. ¹		9–10 d. ¹ 4 d. ²	24–30 h. after coitus (27 h.) ²	— ²	4–8 d.	Usually the 1st estrus or 3–4 weeks after weaning kittens

*Numbers in parentheses are average figures. 1, 2, 3, 4, 5, 6, 11.

¹The cat has several cycles each breeding period. The latter occur usually 2 or 3 times a year if it is not bred.

²The cat does not ovulate spontaneously. If coitus occurs the cat goes out of estrus in about 4 days.

36 hours after the onset of estrus.^{37,38} Migration of the early zygote from one uterine horn to the other horn is fairly common in ewes, mares, bitches, sows and queens but rare in cows. Migration of the ova across the peritoneal cavity of domestic animals has not been reported.

The formation and development of the corpus luteum under the influence of LH results in the production of progesterone necessary for the preparation of the uterus and probably the rapid passage of the zygote through the isthmus into the uterus. Progesterone is also essential to the maintenance of pregnancy. Because of the effect of the blastocyst on the endometrium, the release of prostaglandin is inhibited and LH secretion maintains the corpus luteum. Otherwise in nonpregnant animals starting about 16 days in the cow and sow and about 10 to 12 days in the ewe and mare the corpus luteum would begin to involute resulting in another estrous period 4 to 5 days later. Placement of or spacing embryos in the uterus in multiparous animals occurs during this early embryonic period. The blastocyst elongates rapidly in the cow, ewe, and sow but remains spherical in the mare, bitch and queen. The uterine luminal fluid or "uterine milk" is rich in mucopolysaccharides, protein, free amino acids, salts like an ultrafiltrate of blood plasma supplemented by secretions of the uterine glands. The shedding of the zona pellucida is probably caused by intrinsic factors in the developing blastocyst.^{5,24,25} Normal gestation and zygote passage into the uterus is carefully synchronized. The early loss of fertilized eggs or embryos is usually not recognizable and is called infertility or sterility.

A thorough knowledge of the various physiologic reproductive phenomena of each domestic species is essential in order for the veterinarian to understand and intelligently treat the various causes of infertility and supervise artificial insemination, embryo transfer and reproductive health programs. The knowledge in this basic field is being rapidly advanced and as more information is obtained clinical application of this knowledge and treatment will be based increasingly on facts instead of empiricism.

The basic physiologic reproductive knowledge necessary for all veterinarians on the domestic species is given in Table 17. These are average or mean figures. Individual animal variations and differences are common but as a general guide this information is useful. A more complete discussion of the reproductive cycle, endocrine effects on the cycle and the reproductive physiology of the postpartum period and the reproductive physiology of the postpartum period and the reproductive physiology of the postpartum period will preface each of the following Chapters on female infertility in the various domestic species.

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Chapter XIII

INFERTILITY IN THE COW

It has been estimated by Asdell that sterility and reproductive troubles in dairy cattle in the United States cost \$250,000,000 annually. In New York State these losses annually amount to \$20,000,000 when figured on the basis of data collected on the causes of culling from Dairy Herd Improvement Association herds. Culling of cows on the basis of sterility has increased from 1.1 percent to 2.5 percent in the last 15 years.³ Much of this rise may be accounted for by better recording. In Northeastern United States 12 to 19 percent of dairy cows culled from herds each year were culled because of infertility or sterility.^{104,140,160} The great economic importance of cattle infertility on a world wide basis has been considered.⁴⁵ Artificial insemination, increased productivity of cows, higher costs of raising and feeding cows, and better education of the farmer and veterinarian all have served to emphasize the importance of maintaining the fertility in dairy and beef herds and individual cows.

The control of brucellosis by vaccination and testing, and trichomoniasis by AI, and vibriosis with antibiotic-treated semen and vaccination of cows has greatly reduced the severe problem of contagious genital infections but has focused attention on other causes of abortion and infertility. The increased movement of purebred cattle between states and herds has occasionally resulted in the introduction of an infectious venereal disease that seriously affected the herd's fertility. The widespread use of hormones as aids or cures in treating certain sterility problems has been recognized. With larger herds and greater mechanization of farms, management problems of handling cattle, detecting estrus for artificial insemination, maintenance of records, and nutritional problems are becoming increasingly important. With more veterinarians taking an active interest in this field many farmers are coming to realize the value of the routine preventive health practices of pregnancy and routine genital examinations in maintaining good productive and reproductive levels in a herd.

A well-managed dairy herd should have 60 to 70 percent of the cows conceive on first service with an average of 1.3 to 1.7 services per conception. There should be less than 10 percent of the cows with reproductive "problems." The calving interval from one calving to the

next should be between 12 and 13 months. It has been reported that for every day a cow has failed to conceive beyond 90 to 100 days postpartum it is costing the farmer 1 to 2 dollars. Thus in a poorly-managed herd of 100 cows with a calving interval of over 13 months for every 30 days reduction in the calving interval the farmer would realize an increase in income of \$3,000 to \$6,000 in 1982 dollars.^{87,132} Even in high-producing cows it is necessary to maintain this 12 to 13 month calving interval because in the cow's lifetime there would be more peaks of high production and a greater total production of milk. Furthermore with longer calving intervals the cow is more likely to freshen at the time of year when prices for milk are the lowest and there is a greater chance for culling the cow for economic reasons. In beef herds the cow that fails to conceive during the breeding season is usually culled for economic reasons. Since 95 percent of the variation in calving intervals or breeding efficiency is due to nongenetic reasons, the importance of management and veterinary supervision of the reproductive activities in the herd is obvious.^{40,152}

There is no such thing as a normal infertile cow. Either there is a clinical or nonclinical pathologic cause or the animal has not been properly exposed to fertile semen during an estrous period. In the next section will be a discussion of the reproductive physiology of the bovine animal. This is essential to the understanding of the pathologic causes of infertility and for the devising of management practices that will promote a high level of fecundity.

Bovine Reproductive Physiology

The Bovine Estrous Cycle—The cow is polyestrous and comes in estrum throughout the year. The estrous cycle length in heifers is an average of 20 days with 85 percent of the heifers having cycles of 18 to 22 days. In cows the average length of the estrous cycle is 21 days and 84 percent of the cows have cycles of 18 to 24 days.² The individuality of the animal may affect the cycle length, but the season has no effect on cycle length. In beef cattle the average length of the estrous cycle is 20 days;

79 percent of the cattle have cycles of 17 to 23 days. It was reported that 83 percent of the heifers had estrous periods within the range of 10 to 21 hours in length while 93 percent of the cows fell within the range of 13 to 27 hours.² The average duration of estrus was about 18 hours.^{11,138} Ovulation is spontaneous in the cow and occurs an average of 10.5 to 15.5 hours, average 12 hours, after the end of estrus. This range of time may vary from 2 to 26 hours. Heifers tend to ovulate about 9 hours after the end of estrus. About 80 percent of the ovulations occur from 4 P.M. to 4 A.M.^{2,4}

In Zebu and crossbred Zebu cattle the average length of estrus is short, 4.7 to 7.4 hours, range 2 to 14 hours, respectively.^{1,32,109,113} Zebu cows tend to associate with the bull for a longer period with many of the cattle exhibiting estrus during the night and early morning hours.¹¹⁸ The average duration of estrus in European dairy or beef cattle in tropical countries and in southern states is shorter, 12 to 13 hours, than in the temperate zone.^{32,47,60} **Bos indicus**, Zebu or Indian cattle, or their crosses are more heat tolerant, and have a higher fertility in spring, summer and fall months in the countries near the equator.¹⁷ They tend to be less fertile in the winter months. They seldom come into estrus while nursing their young, possibly for nutritional reasons.³² Brahman cattle have calving intervals of 414 to 554 days.¹¹³ They seldom show heterosexual activity of mounting other cows. Brahman cattle had a lower LH peak at estrus, a smaller corpus luteum and lower progesterone values in diestrus than European cattle.¹¹³ Their gestation periods vary from 271 to 310 days, average 293 days.¹⁰⁹ European cattle, **Bos taurus** or cattle of the temperate zone are less adapted to hot climates.

Three to 6 percent of pregnant cows, especially the first trimester of pregnancy, exhibit signs of estrus and up to 85 percent of these cows were rebred during pregnancy^{49a} (see Chap. II, Pregnancy Diagnosis). In 5970 pregnancy examinations in cows, 59.2 percent were pregnant in the right horn and 40.8 percent in the left. Of 4290 heifers, 54.4 percent were pregnant in the right horn and 45.6 percent in the left horn.¹⁰³ Thus 55 to 60 percent of the ovulations and pregnancies occur in the right ovary and horn. Transuterine migration of the bovine embryo is very rare.

Manual removal of the corpus luteum, which is only possible in cattle, produced estrus in 3 to 5 days, the average time being 4.2 days.⁴ In over 300 Herefords in which the corpus luteum was expressed manually about equal numbers came into estrus on each day from 2 to 7 days.¹⁴ In the author's experience, most cattle show estrus the third day after removal of the corpus luteum and if external symptoms of estrus are not observed,

the animal should be inseminated or bred late on the third day or on the fourth day. Because of the occasional hemorrhages and secondary adhesions or rare deaths, this practice is presently seldom followed as equally satisfactory results can be obtained with a luteolysing dose of a prostaglandin with the onset of estrus occurring in the same time period as manual removal of the corpus luteum.

The symptoms of estrus in the cow are characterized by a great amount of homosexual behavior. Normal and abnormal estrous behavior patterns in cattle have been described.^{44,46,59}

The amount of sexual activity is generally related to the amount of estrogen present but in a few ovariectomized animals estrogen failed to produce symptoms of estrus possibly due to a lack of progesterone since the latter is synergistic with estrogens in producing signs of estrus.^{4,93} There are great differences in individuals in the intensity of estrous symptoms exhibited. Heifers usually exhibit more marked symptoms of estrus than do cows. When artificial insemination is practiced and a bull does not run with the herd, careful observation of cows by the owner or herdsman twice a day or more often at non-feeding periods is essential for the maintenance of a satisfactory breeding program. The onset of estrus was gradual over a period of several to 24 hours in 66 percent of the cows and heifers, and abrupt in 34 percent.¹¹⁵ Animals in the "coming in" stage of estrus were often restless, raised and twitched their tails, discharged some milky-colored mucus from the vulva and often associated with a larger or more aggressive cow. This "coming in" stage was more noticeable in heifers.

The cow in estrus is usually restless and often remains standing rather than lying down. The appetite, ruminations, and milk yield may be slightly decreased. Bellowing is frequent especially if the cow is separated from the herd. The cow in estrus will attempt to mount other cows and will stand to be mounted by others cows. This latter sign of standing to be mounted is the most significant and important sign to observe in the detection of estrus. This characteristic immobility or willingness to stand without moving for the male to mount and complete the copulatory act is the cardinal sign of estrus in all domestic animals, cow, mare, ewe, doe, sow, bitch and queen.

Although the vulva of the cow in estrus was sniffed by other cows, the cow in estrus was never observed to sniff the external genitals of the other cattle.¹¹⁵ The heterosexual and homosexual behavior of the cow in estrus was always more intense than that of its partners. The tail may be raised and there is often a long string of clear mucus hanging from the vulva or present on the

tail or buttocks. The vulva is usually somewhat congested, flaccid, edematous, and relaxed. The cow in a stanchion tends to hold her head high and has an alert, interested, even inquisitive, attitude. The cow may urinate frequently. Three to 6 percent of cows, with occasional reports as high as 14 to 18 percent of cows showed signs of estrus after conception.^{39,60,112} This occurred most often the first trimester of the gestation period over a range of 11 to 213 days with a mean of 63 days.

On vaginal examination the vaginal mucosa, especially the cranial portion, is congested and slight edematous. The large amounts of stringy mucus, 50 to 100 ml., present in the vagina at estrus comes from the vaginal and cervical mucous cells under the influence of estradiol.⁸⁸ At the time of estrus the viscosity of the mucus is lowest, and its flow elasticity greatest. When estrous mucus is smeared thinly on a slide and dried the high salt or NaCl content crystallizes into a fern or arborization pattern. The external os of the cervical canal is usually pink, congested, edematous, and slightly relaxed and open at the time of estrus. The cow in estrus seldom objects to and usually stands well for a vaginal examination. The vaginal speculum slips in easily due to the viscid mucus present in the vagina. Vaginal smears during proestrus and estrus show increased numbers of cornified cells, but variations between cows are so great that the vaginal smear in the cow cannot be regarded as a reliable indication of estrus. During diestrus the vagina is pale and dry and the mucus is scant and rather sticky. The speculum therefore passes with greater difficulty than during estrus.

On rectal examination during estrus and for 1 to 2 days before and afterwards, the uterus is usually erect, turgid, and somewhat edematous due to the estrogenic stimulation of the uterine muscle and tissues. This is most noticeable in heifers. Usually 1 to 5 smaller follicles start development but undergo atresia during estrus and after ovulation. On rectal palpation early in estrus the ovarian follicle is about 1 cm. in diameter or less, and smooth, convex, tense and slightly fluctuating due to the follicular fluid present. This fluid is amber in color. The maturing Graafian follicle before rupture is 10 to 20 mm, or 1 to 2 cm, in diameter. At the time of ovulation in the cow only a very slight amount of bleeding occurs at the rupture site.

The corpus luteum develops rapidly from the granulosa and theca cells of the collapsed follicle under the tropic influence of LH from the pituitary gland. By 48 hours after ovulation the corpus luteum is about 1.5 cm in diameter and slightly crepitant on palpation per rectum. By 7 to 8 days after ovulation the corpus luteum

has reached its maximum size of 2 to 2.5 cm. in diameter. The corpus luteum in the cow is irregular in shape, usually oval, and with a cone-like projection about 1/2 to 1 cm. above the surface of the ovary. The corpus luteum of estrus weighs from 4.1 to 7.4 grams and is nearly similar in size and weight to the corpus luteum of pregnancy.¹² The size of the corpus luteum based on manual palpation and observation on laparotomy at 7 to 8 days postestrus has no correlation with progesterone production or plasma progesterone levels.^{113c} The corpus luteum of pregnancy decreases in size just before parturition but may be palpable for many months after parturition as the corpus albicans, a small fibrous structure, on the ovary. The mature corpus luteum is brownish yellow to yellow orange in color, giving it the common name of "yellow body." In about 25 percent of the corpora lutea there is a small cavity about 0.4 cm. in diameter. In a few cases large cavities 1 cm or more in diameter, filled with an amber fluid may be present.^{4,12} These corpora lutea containing large cavities are spoken of as cystic corpora lutea. Cystic corpora lutea have not been observed in a cow in the last third or half of the gestation period.⁷⁹ Graafian follicles that failed to ovulate but became partially luteinized are called luteal cysts. These pathologic luteal cysts have a smooth convex surface due to the thick-walled fluid-filled follicle that failed to ovulate. While the cystic corpus luteum follows a normal ovulation and although it contains a variable amount of fluid in its center, lutein tissue protruding through the site of ovulation produces an irregular, raised area on the surface of the ovary.¹² Normal corpora lutea are irregular in outline and have a liver-like consistency. Cystic corpora lutea are similar to normal corpora lutea on palpation except they are usually larger, more spherical and fluctuate on pressure. The cystic corpora luteum is not considered to be pathological but the luteal cyst is pathological. The corpus luteum maintains its size until about 48 hours before estrus, after which time its size diminishes rapidly. Its color at this time of rapid involution is light orange to yellow. By 48 hours after estrus its size is about 1 cm. and by about 10 days after estrus 0.5 cm.¹² As it becomes older its color turns to dark orange and then brick red. This eventually becomes a small white fibrous area the size of a large pin head, the corpus albicans. On rectal palpation, when one ovary is definitely larger than the other the difference is usually due to the presence of a corpus luteum in that ovary. Cysts may also cause this discrepancy in size.

In cows, body temperatures taken deep in the vagina were lowest just before estrus, high on the day of estrus due to the cow's activity, low at the time of ovulation and high during the luteal phase of the cycle as in

women.¹⁷⁰ Determining body temperature changes, the glucose content, or the arborization or fern pattern of cervical mucus were not practical tests for indicating estrus or heat and the time to breed cattle.^{9,75,170} Direct visualization of the ovaries of cattle during the estrous cycle by endoscopic methods has been reported.^{8,92}

About 15 to 36 hours after ovulation, about 24 to 48 hours after estrus, or about 40 to 60 hours after the onset of estrus a discharge of blood and mucus from the vulva may be observed in many cows. This metrorrhagia from the edematous endometrium in the caruncular areas occurs due to a breakdown of congested capillaries. Although clinical evidence of bleeding occurs in only 80 percent of heifers all show the presence of red blood cells on examination of vaginal swabbings at this time.¹⁵⁹ Metrorrhagia in cattle was observed in about 75 percent of heifers, and 48 percent of cows.⁴ In any particular animal clinical bleeding may not be observed following every estrus.

It is a common belief amongst a few farmers that post-estrous bleeding following service is an indication that conception did not occur. In 100 heifers that were bred, 81 showed clinical prostestrous bleeding. Eighty-five percent of those that conceived bled, and of those that did not conceive, 74 percent bled. In another group of 100 cows, 61 bled and 69 percent of those that conceived bled, and of those failing to conceive, 39 percent showed metrorrhagia.¹⁴¹ The metrorrhagia that occurs in cattle is not similar to menstruation in primates, as it occurs at the end of the estrogenic phase of the cycle or early metestrus, following estrogen withdrawal. While in primates bleeding occurs at the end of the luteal phase of the cycle or the end of diestrus, following progesterone withdrawal.⁶⁵ Small perimetrial hemorrhages in the subserosa of heifers' uteri were commonly seen from estrus to the fourth day postestrus. Hemorrhages of this nature were not observed in pluriparous cows.¹⁵⁹

Optimal service time—Insemination of cattle between 8 to 24 hours, or especially 7 to 18 hours, before ovulation results in the highest rates of conception.¹⁴⁶ Ovulation should occur in heifers in the temperate zone about 22 to 36 hours after the onset of estrus. Conception rates were still better than 50 percent from service more than 24 hours before ovulation, if the cow was in estrus, to within 6 hours of ovulation. Conception rates drop rapidly in cows bred after ovulation or after 10 to 18 hours after the end of estrus.^{20,138,146} In other studies^{11,146} conception rates of cows inseminated about 10 hours after the onset of estrus was about 82 percent; at 20 hours after the onset of estrus or soon after going out of estrus 62 percent; by 30 hours after the onset of estrus or near the expected ovulation time, the concep-

tion rate was 28 percent. This rate dropped rapidly so that by 50 to 60 hours after the onset of estrus very few cows conceived. However, a conception rate of 20 to 30 percent was reported if cattle were inseminated while they were showing metrorrhagia and a bloody mucous discharge.^{7,85} Based on the above data, the best time for insemination is from just before the middle of estrus to 6 hours after estrus or from 6 to 24 hours after the onset of standing estrus.^{103b} (See repeat-breeding cows.) In 7,346 dairy herds in which 455,196 cows were artificially inseminated in one year the nonreturn rate of 66 percent was similar for cows serviced once a day at about the same hour, once a day either in the A.M. or P.M. or twice a day with cows observed in estrus in the A.M. serviced that P.M. or cows in estrus in the P.M. being serviced the next A.M. When the herd size was 20 to 50 cows, 51 to 100 cows, 101 to 150 cows and over 151 cows the nonreturn rates were 68, 66, 64 and 62 percent respectively. Cows in loose housing had a 64 percent nonreturn rate compared to 67 percent in tie or stanchion housing.^{103b}

Although the possibility of conception may be somewhat less in cows with shorter- or longer-than-normal cycles of 17 to 25 days, many of those cows do conceive when they are bred.¹⁴⁹

Intravaginal deposition of semen in artificial insemination gives poor conception rates because of the small numbers of spermatozoa deposited. The rectovaginal technique for introducing semen into the cervix was superior to the speculum technique with about 16 percent better conception rate.¹⁴⁹ Deposition of semen in the cranial cervical canal gave equally as good results as semen deposited in the uterine body or horns and the technique was simpler. Because the endometrium is easily injured, and infection and occasional abortion may result from intrauterine deposition of semen in pregnant cows, and since about 3.5 to 6 percent of pregnant cows show estrus, it has been recommended that cervical deposition be used instead of the uterine deposition of semen.¹⁴⁹

Hormones of the Estrous Cycle—The level of hormones in cattle, with the possible exception of LH, are low in comparison to other domestic animals. In recent years highly sophisticated assay techniques have been devised that have further delineated the hormonal control of the estrous cycle in cattle. The subject of hormone levels in the reproductive endocrine glands and the blood plasma at different stages of the estrous cycle and during pregnancy was reviewed.^{25,116,156} Follicle stimulating hormone (F.S.H.) plasma levels range from 300 to 550 ng/ml., with low values for 3 or 4 days after estrus and higher values at estrus coinciding with peak values of luteinizing hormone (LH). Luteinizing hormone (L.H.)

plasma levels range from 1-1/2 to 3 ng/ml. produced by frequent daily episodic fluctuations or pulses with a gradual rise to 4 or 5 ng/ml. just before the next estrus with a very high peak, the LH surge, of 11 to 15 ng/ml. early in estrus that lasts for only a few hours.

Progesterone levels in plasma average 5 to 7 ng/ml. (range 4 to 9 ng/ml.) during the midcycle from 6 to 19 or 20 days when two to three days before the next estrus regression or involution of the corpus luteum occurs rapidly under the influence of prostaglandins from the endometrium and possibly the corpus luteum and progesterone levels fall below 1 ng/ml. during estrus and then slowly rise to normal diestral levels by day 6. Following superovulation in the cow progesterone levels in the last milk rose from 8.2 ng/ml. at midcycle to 52.6 ng/ml. and correlated with the number of ovulations and embryos recovered.^{43a}

Estradiol levels in plasma average 2 to 7 pg/ml. from the day after estrus with a slight peak at midcycle to 2 or 3 days before the next estrus when the estradiol level rises and reaches a peak early in the next estrus of 10 to 20 pg/ml., after which it falls rapidly.

An excellent recent review of the physiology and endocrine control of the estrous cycle of domestic food-producing animals has been published.^{66b} The role of oxytocin in luteolysis is discussed in light of the recent observation that oxytocin is present in considerable concentration in the bovine corpus luteum where it is probably synthesized. Large quantities of arachidonic acid, a prostaglandin precursor, is also found in the corpus luteum as well as the uterine endometrium. Recent studies have shown that PGI_2 is luteotropic and $\text{PGF}_{2\alpha}$ is luteolytic. Thus a balance of these two prostaglandins may determine the functional state of the bovine corpus luteum. The presence and release of oxytocin from the bovine ovary during the estrogenic phase of the estrous cycle may be responsible for the greatly increased tone of the uterine musculature characteristic of estrus in the bovine species.

The blood plasma levels of certain reproductive hormones during the bovine estrous cycles are generally quite different from those during the gestation period when F.S.H. and L.H. are low, the latter about 1.0 ug/ml. Progesterone levels are about the same as during diestrus and decline to very low levels at parturition. Estrogen levels rise during late gestation to a peak at parturition of 3000 to 5000 pg/ml. total estrogen. The half-life of the progesterone in the blood in cattle was short, about 10 to 20 minutes, indicating the need during the estrous cycle and pregnancy for a continuous large supply.⁷⁶ Normal corpora lutea in pregnant heifers at 15 days after insemination contained an average of 270 mg. total pro-

gesterone and no pregnant heifers had less than 100 mg. which was the minimum necessary for embryo survival.¹³⁶

In ovariectomized cows conditioned with 0.2 to 0.4 mg of estradiol/1000 lbs, 1 to 4 mg of progesterone would produce maximal synergistic action with the production of typical estrum lasting 6 to 12 hours.⁹³ Both of these hormones necessary for typical expression of estrus are produced in the ovary during the preovulatory development of the follicle. The CL from the previous cycle contains measurable progesterone for several days after estrus.⁵⁴ Large doses of progesterone 30 to 60 mg. antagonized or prevented estrous behavior in estrogen-treated ovariectomized cattle.

Puberty and the onset of estrous cycles (See Chapter 12)—As discussed previously placing young heifers on a nutritious diet high in TDN from birth can hasten puberty and the onset of estrous cycles. This can also permit heifers to be bred successfully at a younger age if they are continued to be fed well during the first gestation period. Breeding heifers on the basis of body weight is therefore indicated, so that heifers can calve at about 2 years of age without serious calving problems. Crossbred heifers tend to show estrus a month or so earlier in life than the parent breeds. Depending on the level of nutritional intake, heifers first show estrus from 7 to 18 months or 28 to 72 weeks of age. In 53 Holstein heifers the time after birth at which first estrus occurred was more variable than the weight which averaged 42 weeks and 610 lbs., respectively.⁹⁶ During the prepuberal period most heifers had one or more follicles with a diameter of 0.5 to 2 cm. and showed evidence of increased follicular activity about 20 to 40 days before the first ovulation. Variable signs of estrus were observed at these times. At the first estrus 74 percent of the heifers exhibited "silent" estrus, or failed to show signs of estrus. This percentage dropped to 43 percent the second estrus and 21 percent the third estrus. Thereafter the estrous periods and signs were normal. Ovulation failed to occur in 13 percent of 53 heifers after the first estrus but thereafter failure of ovulation was rare. Nearly similar results were reported in 37 Holstein heifers in a later study.¹⁰¹ Heifers should be of sufficient age and weight to reach puberty prior to any hormonal treatment to induce or control estrous cycles if acceptable pregnancy rates are desired.^{132b}

The postpartum period and the onset of estrous cycles—A review of the literature on postpartum ovarian activity and uterine involution indicated the interval from parturition to first observed estrum varied from 30 to 76 days in dairy cattle and 40 to 48 days in beef cattle.^{98,99,100} The time required for uterine involution based on rectal palpations and clinical observations and mea-

measurements varied from 26 to 52 days in dairy cattle and 38 to 56 days in beef cattle. In general the interval from calving to first estrus was greater in cows with higher production, in cows nursing calves or being milked 4 times a day, in cows on a poor or low level of nutritive intake, and in older pluriparous cows with 4 or more parturitions.^{121,157} A longer postpartum interval to first estrus occurred in nursed dairy cows, anemic cows and in those being fed thyroprotein.

When Brahma-Hereford heifers were allowed to suckle their calves only once a day, starting at postpartum day 30, the postpartum interval to first estrus was 69 days average vs 168 days for control heifers that suckled their calves normally. These times were shortened to 32 and 124 days when the experiment was started at 21 days postpartum and the level of nutrition was increased.^{113b} This relationship of nursing and the delayed onset of estrous cycles after calving was further reported upon.¹⁶⁵

Involution of the uterus was prolonged in pluriparous cows when compared to primiparous cattle and also in abnormal parturitions characterized by dystocia, retained placenta, twinning, metritis, milk fever, displaced abomasum and other disease or stress factors. Ovariectomy and physiologic doses of estradiol had no effect on uterine involution but progesterone delayed uterine regression.⁹⁰ However others⁴³ reported that progesterone and estradiol somewhat shortened the intervals to ovulation and conception. Thus uterine involution proceeds normally even if reproductive cycles and estrus do not occur. Exogenous estrogens or progesterone, ovariectomy, or nursing calves have little or no effect on the rate of uterine involution.¹³³ Sloughing of caruncular tissue occurred between 7 and 14 days postpartum and by 30 days the surface epithelium over the caruncular areas were regenerated.¹⁵⁷ Normal cows usually develop a mature follicle that ovulates and is followed by the formation of a corpus luteum at 13 to 15 days after calving.^{89,98-100,157} The duration of the estrous cycle from the first ovulation to the second ovulation was 3 to 4 days shorter than the normal length cycles, 20 to 21 days, that followed thereafter. "Silent" estrus occurred in 77 percent of the first postpartum ovulations, 54 percent of the second and 36 percent of the third ovulations, and was more common in high-producing cows.⁹⁸⁻¹⁰⁰ Cystic corpora lutea and cystic follicles were fairly common and a failure of ovulation occurred occasionally in up to 10 percent of the cycles.²¹ Ninety percent of the first corpora lutea developing within 15 days after calving formed on the ovary opposite to the previously gravid horn; this percentage dropped to 60 percent in cows ovulating 15 to 20 days after parturition.⁸⁹ The corpus luteum of pregnancy had regressed at 4 days postpartum to 1×1.5 cm in size

and was usually not palpable after 14 days postpartum.

Uterine involution in normal cows is largely completed as indicated by the size of the uterus and the condition of the endometrium at about 30 days postpartum and since normal estrous cycles are usually occurring by 30 days after calving^{98-100,157} it is logical to ask whether it might not be feasible and practical to commence breeding a month before the generally previously recommended minimal time of 60 days postpartum.

In the early 1950's a number of studies conducted on early postpartum breeding of dairy cows indicated that breeding cows prior to 60 days resulted in conception rates below 50 percent, an increased number of services per conception and even prolonged the postpartum interval to conception with adverse effects on the subsequent pregnancy and parturition.^{74,125,142-146}

Subsequent studies on large numbers of cows showed that conception rates per service in cows bred 20 days or less postpartum average 18 percent, those bred 20 to 40 days averaged about 35 to 45 percent, from 40 to 60 days postpartum about 50 to 60 percent. A definite increase in number of services per conception occurred in cows bred prior to 50 days postpartum. These early bred cows had a shorter calving interval, often averaging 11 to 12 months, due to a reduction in days from calving to conception. There was no evidence that early postpartum breedings were associated with an increased incidence of delayed returns to estrus, infertility or subsequent abortions or retained placentas.^{15,42,57,106,131b,137a,161,162}

Since the optimum calving interval for maximum daily milk production in high-producing dairy herds is controversial and since for high milk production a dry period of 42 days or more is essential,⁴² a somewhat flexible management program is indicated based on the age and productivity of the individual cow, the ease of calving and the presence or absence of periparturient disease and the evaluation of the recovery or involution of the genital tract based on routine postpartum rectal examinations. Two and three-year-old cows had a 61 percent postpartum first service conception rate. Cows 4 years-old and older had only a 35 percent conception rate on first service postpartum. The occurrence of one or more postpartum diseases reduced the first service conception rate and milk production was negatively correlated with conception.^{137a} A desirable goal of a calving interval of 12 to 13 months in a high-producing herd translates into a postpartum "open" interval of 85 to 115 days, respectively, for all of the cows in a herd. Having many cows over or under these figures in order to arrive at a desirable average figure should be regarded as poor management. Further information on this important postpartum period will be discussed later in this chapter.

Conception rates for estrous cycles of less than 18 days in length were poor, about 34 percent, in cows not bred at the previous estrus.^{38,145} Increased calving intervals in dairy and beef cows often occur after they reached 5 years of age or after their fourth lactation period.

Physiologic utero-pituitary-ovarian relationships and the luteolytic mechanism controlling the estrous cycle—The corpus luteum, follicle, and the placenta are the only three transitory endocrine glands. The understanding of the mechanisms controlling the formation and involution of the corpus luteum is essential. The corpus luteum is present and active in the fertile cow for about 320 days a year. It only involutes long enough in the normal cow to permit a follicle to mature and ovulate in order to perpetuate the species. The presence of a functioning corpus luteum on the ovary is of much more significance than various stages of follicular development or atresia.

Although more work is required to explain certain aspects of the utero-pituitary-ovarian relationships, the major aspects of this relationship have been reviewed.^{50,51,133} It is generally accepted that LH which is the principal luteotropic hormone in the cow¹²⁸ is released from the anterior pituitary gland to produce ovulation; corpus luteum formation from the granulosa and thecal cells; corpus luteum persistence; and secretion of progesterone necessary for suppression of follicle growth, early embryonic growth, development and attachment, and for the maintenance of normal pregnancy. The presence of the embryo with its elongated trophoblast is necessary by about the 14th day of the cycle to prevent the involution of the corpus luteum which starts, in the absence of the embryo, about the 15th or 16th day of the cycle. The process causing the regression or involution of the corpus luteum of the estrous cycle to permit Graafian follicle development is called the luteolytic mechanism. This releases prostaglandin F_{2a} from the endometrium in the absence of the substance or hormone from a developing blastocyst.¹⁰ This mechanism of estrous cycle regulation is more complex than realized ten years ago and possibly involves a balance or interaction between ovarian steroids, gonadotropic hormones and the luteotropic action of prostacyclin early in the cycle⁹⁴ as well as other unknown influences. If conception has occurred the conceptus prevents the release of prostaglandin and the resulting involution of the corpus luteum and causes pregnancy to be maintained. In the cow the prostaglandin from the endometrium is carried to the ovary by the local utero-ovarian pathway.⁵² Many studies influencing and elucidating but not completely explaining, the luteolytic mechanism have been performed.^{52,116}

Thyroidectomized or parathyroidectomized cows were

fertile and could carry fetuses to term and rebreed. Low fertility associated with high environmental temperatures was not associated with depressed thyroxine secretion rates.¹⁶² There was no evidence that feeding iodinated casein caused infertility, even after 2 years of continuous feeding. The thyroxine secretion rate in dairy cattle was 67 percent higher than in beef cattle.¹⁰⁸ Adrenal function in relation to reproduction was reviewed in relation to ovarian inactivity, cystic ovaries and prolonged or shortened gestations.^{151,155}

Other endocrine effects—Typical signs of estrus can be produced both clinically and on vaginal and rectal examination in an ovariectomized heifer by the daily injection for 3 days of 0.10 mg. of estradiol or 0.25 mg. of stilbestrol.⁵ Thus it makes more understandable the reason why massive therapeutic doses of 4 mg of estradiol and 40 mg of stilbestrol, greatly exceeding the physiologic dose, can cause cystic ovaries.

Other associated endocrine phenomena related to the uterine luteolytic mechanism and uterine-pituitary-ovarian physiology include the following.⁴⁹⁻⁵¹ Exogenous estrogens, such as 5 mg estradiol valerate or injections of estradiol having a prolonged effect, given to cattle at midcycle caused early CL regression.^{18,166} This is probably due to an interference with LH release since concurrent injections of gonadotropins prevent the regression of the CL. Exogenous estrogen is luteolytic and levels of FSH and LH that promote increased estrogen secretion might also promote luteolysis.⁶⁸ Daily exogenous injections of 100 IU of oxytocin days 2 to 6 after estrus caused the failure of the corpus luteum to develop with an early return to estrus and a short cycle of 10 to 14 days.^{18,35,37} The author has observed this as a cause for repeated short cycles and infertility when the owner of a high-producing cow gave repeated daily injections of oxytocin to cause milk "let down." These short cycles are due to the release of prostaglandins from the uterine endometrium by the exogenous oxytocin and the subsequent luteolysis is produced by the released prostaglandins.^{94b} Adrenocorticotropin (ACTH) 100 units daily on days 2 through 8 of the cycle significantly reduced CL weight. The effect of ACTH on the adrenal gland to produce corticosteroids that can cause abortion as well as uterine involution is noteworthy.¹⁸ An injection of LH in an adjuvant at midcycle or daily injections of HCG starting at day 15 prolonged the life of the CL and increased estrous cycle length in cattle.^{164,167} Although these injections of HCG caused accessory corpora lutea to develop, it had no effect on embryo survival. Thus, as expressed by Short¹²⁷ the CL can be "murdered" by the local effect of the uterine luteolysin prostaglandin on the CL; it can be "starved to death" by the removal of the

tropic stimulus, LH, due to the systemic effect of prostaglandins and estrogens on the hypothalamus and pituitary gland; or the CL can die of "old age" since the CL in each species has a finite life span.

Synchronization of Estrous Cycles or Ovulation

Control—Estrus synchronization or control of the estrous cycle and ovulation whereby one to many heifers or cows in a beef or dairy herd could be brought into estrus at a specific time is highly desirable from a practical, economic standpoint to breed cows artificially to proven sires, to shorten the breeding season and cluster calvings, and to improve estrus detection. Manual removal of the corpus luteum per rectum was a common practice for producing estrus until recently. (See Section on Anestrus.) This practice frequently produced bleeding, adhesions and ovarian damage with occasional hemorrhage and deaths. The first endocrine products available and used for this purpose were stilbestrol and other estrogenic products. These products could produce signs of estrus within 24 hours after injection but since a physiologic estrus and ovulation did not occur conception rates were extremely low and occasionally cystic ovaries were produced. The gonadotropic hormones became available and results in inducing estrus were poor, the costs of the drug high, and occasionally superovulation or anaphylaxis was produced.

About 25 to 30 years ago progesterone and progestins became available that by injection or feeding would suppress the gonadotropic hormones and the estrous cycle for long periods of 20 to 25 days during which the corpus luteum would involute. When the progesterone or progestins were withdrawn estrous cycles with ovulations would occur within the next 2 to 6 days. However conception rates at this controlled estrus were too low, 15 percent below controls, to be of practical or economic value.⁶⁶ Many hundreds of experiments with many hormones, such as estradiol and gonadotropic or GnRH hormones in combination with progesterone have been performed to improve synchronization and fertility with equivocal or little success. The two most promising of these current experimental procedures for synchronizing estrus involve a short term exposure to progesterone of 7 to 9 days. One treatment consists of an estradiol injection at the time of implantation of a progestogen, (Syncromate-B) or norgestomet (Searle) under the skin of the ear of heifers or lactating cows that is removed 9 days later.^{66,80,131} This procedure has been combined with the administration of prostaglandins on day 7 or with removal of nursing calves for 48 to 60 hours. (Shang treatment.)^{26,78,131} The second treatment is to insert a progesterone releasing intravaginal device (PRID) followed by the injection of a luteolytic dose of prostaglan-

din the day before removal of the PRID on the seventh day.⁶⁶ This experimental treatment resulted in 76 percent of the heifers being in estrus within a 24 hour period. This degree of synchrony is important for AI. Conception rates were about 80 percent for both treated and control heifers in which estrus detection practices were excellent and heifers were bred 12 hours after estrus was observed. In another report 44 cyclic Holstein heifers were synchronized with a PRID and 10 mg estradiol benzoate. The PRID was removed 12 days later and 2 days thereafter 84 percent of the heifers were in estrus and bred by fixed AI 56 and 74 hours after PRID removal with a 63 percent conception rate.^{82b} Further studies are indicated. Currently only the former of these latter three treatments with steroid or progesterone components have been approved for use in the U.S.

Within the last 5 to 10 years many experimental trials have been conducted to control the estrous cycle with prostaglandins F_{2a} and its analogues.⁶⁶ When a luteolytic dose of prostaglandins is injected between days 5 and 16 of the estrous cycle, estrus and ovulation follows within 3 to 6 days. They are ineffective when given the first five days of the cycle.⁶⁶ Currently these products are approved for use in beef cattle, dairy heifers and dairy cows. Increased concentrations of PGF_{2a} or its metabolites can only be detected in the first milking after treatment.^{66,129} Many varied treatments or procedures have been used in synchronizing heifers and cows with the prostaglandins (Lutalyse, (PGF_{2a}) 20 to 35 mg. IM or 5 mg. intrauterine) or an analogue (Estrumate or closprostenol, 0.5 mg or 500 ug IM). Some protocols of these treatment procedures include:

(1) Heifers are observed carefully for 5 days and bred about 12 hours after estrus. On the fifth day the remainder of the heifers are given a single dose of prostaglandin and these are observed and bred similarly during the next 4 or more days. Conception rate for control heifers was 74 percent and for treated heifers was about 60 percent.⁶⁶ Other experiments have utilized breeding by bulls or timed inseminations, either once at 60 to 80 hours, or twice at 72 and 96 hours. If estrus occurs late on the second or early on the third day after the injection of prostaglandin earlier breeding than 72 hours is indicated. If a cow shows estrus the day after breeding at 72 hours she should be rebred to get the best conception rates. The best results were obtained when the heifers or cows were bred 12 hours after estrus was first observed.^{16,19,28,66,80} A recent report using 12.5 mg PGF_{2a} by this system was superior to (2) as more cows showed estrus, 65 vs 43 percent, respectively and the cost was lower. Breeding based on observed estrus was superior to timed insemination.^{32b}

(2) All heifers were injected with prostaglandin twice 11 days (10 to 12 days) apart to attempt to synchronize all heifers and then bred to bulls or with AI on observed estrus or at timed inseminations either single services at 60 to 80 hours, or double services at 60 to 72 and 80 to 96 hours.^{16,28,80}

(3) A variation of the treatments used in (1) or (2), especially for herds with many unobserved estrus periods, would be to rectally examine all heifers and cows every week and treat those that are nonpregnant with a mature corpus luteum and breed on both observed estrus and at a timed insemination unless they coincided within a few hours.^{123,124}

(4) Inject all heifers and breed on observed estrus. Those not in estrus after the first injection would be given a second injection in 10 to 12 days and bred at observed estrus or on a timed insemination.^{16,19,28,80}

(5) Many other variations and procedures can be used to assist or improve results including careful observation for estrus at frequent intervals, every 4 hours, from 2 to 5 days after injection, and the use Kamar or other heat detection devices. The use of GnRH or a small dose of estradiol to promote the LH surge after giving prostaglandins has not proven to be of value.⁶⁶

Recent studies on estrus synchronization have shown that 10 to 25 percent of beef cows and heifers were not detected in estrus within 5 days after PGF_{2a} administration due to failure of regression of the CL, or the CL regressed but estrus was not observed or estrus occurred 7 to 10 days after PGF_{2a} injection. PGF_{2a} was less effective in regressing the CL between days 4 and 9 of the cycle than later in the cycle.^{81b} It was also noted that the interval to estrus after PGF_{2a} treatment was affected by season, age of the female (shorter in heifers), breed and plasma progesterone level at treatment.^{81b} Estrus response following the first PGF_{2a} injections was low, 45 to 50 percent, in 6 beef breeds and the pregnancy rate after PGF_{2a} injections was poor, 20 to 35 percent, in the Brahman and Brahman-crossbreed cattle, compared to Angus, Hereford and Simmental cattle, 60 to 65 percent.^{148a} In two groups of dairy heifers injected with PGF_{2a} between 6 to 10 days and 11 to 16 days of the cycle response rate was 59.3 vs 95.6 percent respectively and the conception rate was 50 vs 74 percent respectively.^{158a} Prostaglandin injection had no adverse effect on fertility. In 2000 cows bred within 24 hours after the onset of induced and observed estrus, conception rate was 69 percent compared to 60 percent in untreated herdmates.^{91b} The interval from PGF injection to the onset of estrus is often too variable to result in high pregnancy rates with set-time inseminations. Prostaglandin injections can be highly beneficial in cycling dairy cows with unobserved

estrus to achieve conception in a minimum time period.^{96b}

It is important to realistically assess an owners managerial ability. The use of prostaglandins will not "cure" or alleviate infertility due to underfeeding, infectious venereal diseases, defective or poor semen, improper insemination practices, poor records, a lack of observation of estrus, a lack of, or improper identification of animals, and a lack of cattle handling facilities. If prostaglandins are given to pregnant cows or heifers especially under 150 days after gestation, they usually will abort. Thus the status of the cows and heifers in the herd, the degree of managerial ability and organization are vital to successful estrous synchronization. It is unfortunate that usually the herds deficient in this organization are the ones that request or expect a "one-shot" cure. If 70 percent of the properly synchronized estrus periods and ovulations are observed and the conception rate at that service is 60 percent there will only be 42 percent conceptions in the treated animals. A conception percentage above this level requires healthy cattle and excellent management as rates below this figure are commonly experienced in herds attempting estrus synchronization.

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Bovine Reproduction Physiology

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INFECTIOUS DISEASES CAUSING INFERTILITY IN COWS

The infectious reproductive diseases of cattle may be divided into the systemic diseases such as tuberculosis, which occasionally or rarely may affect the reproductive organs, and the more important venereal diseases which infect the genital tract such as: trichomoniasis, vibriosis, brucellosis, and possibly mycoplasmosis and ureaplasmosis. Granular venereal disease, infectious pustular vulvovaginitis due to the IBR-IPV virus and other miscellaneous infections may also affect the reproductive tract and fertility. It is significant that in trichomoniasis, vibriosis and brucellosis a local immunity develops in the genital tract and antibodies may be found in the vaginal mucus for variable, but not prolonged, periods. Any combination of these infectious diseases may occur simultaneously in an animal or herd. A recent review detailed our present knowledge of the reproductive tract, including the reproductive hormones, as a component of the secretory immune system.^{68b}

Trichomoniasis

Definition—Trichomoniasis is an insidious venereal disease of cattle characterized by infertility, early abortion, and pyometra and is caused by the protozoan, *Tritrichomonas fetus*, transmitted to cows by the chronically-infected bull.

Etiology—According to Morgan this disease was first described by Kunstler in France, in 1888, but Mazzanti of Italy in 1900 is generally credited with the discovery. Because of the widespread interest in the discovery in 1897 of Bang's disease, or contagious abortion, apparently little or no work was done on trichomoniasis until the 1920s and 1930s.⁵ In 1932 trichomoniasis was found

in Pennsylvania by Emmerson and since that time the disease has been found in nearly every state in the United States and has been worked on intensively by many investigators. Trichomoniasis has been reported in many countries throughout the world. In Wisconsin, where trichomoniasis was a problem 1,577 bovine uteri from a local packing plant for trichomonads were examined.⁵⁷ Of 997 pregnant uteri only 2 were positive. Of 580 non-pregnant uteri there were 100 cases of pyometra and 13 percent were positive for *Tritrichomonas fetus*. In 9 infected herds involving 800 cattle, it was conservatively estimated that the losses totalled \$200,000 due to loss of potential milk and calves and loss of value of the infected sires.⁷ In recent years trichomoniasis has been diagnosed in the U.S. more frequently in beef herds and less frequently in dairy herds probably due to the extensive use of artificial insemination in dairy cattle. Trichomoniasis is a major contributor to poor calf crops (50 percent) and prolonged calving seasons in beef herds.^{24a}

The results of a survey of 828 western range bulls in 34 herd associations for trichomoniasis showed 7.5 percent of the bulls and 26 percent of the associations were infected.⁴² In two other recent studies 7.8 and 7.3 percent of range beef bulls were infected with *T. fetus* in Oklahoma and Florida.^{6,68} The disease has also been described in range cattle in Australia.²⁵ Since 1940 over 10 A.I. Studs in the U.S.A. have experienced outbreaks of trichomoniasis in their bulls.^{12,32} Beef herds, dealers' herds, valuable purebred herds, and institution herds that frequently change or purchase bulls and cows, are those in which trichomoniasis is most likely to appear.

The causative agent of this disease, *Tritrichomonas fetus*, is a flagellated protozoa with a pyriform or pear-like body. Three small flagella are located at the cranial end of the trichomonad. An undulating membrane extends the length of the body and terminates in a single caudal flagellum. The organism varies from 10 to 25 microns in length and 5 to 10 microns in width. A red blood cell is 5 to 7 microns in diameter. It is about one-third larger than the head of a bovine sperm cell. In fresh preparations the organism is actively motile, exhibiting a jerky, twisting, irregular, spiral continuous rolling and erratic type of movement.^{1,52} Progressive rapid forward movement is seldom observed. *T. fetus* is rapidly killed by drying, by the presence of antiseptics, excessive heat and by other adverse conditions or environment. Once dead it quickly loses its shape, so that it is difficult to distinguish from cellular debris. A common type of vaginitis in women is caused by *T. vaginalis*, an organism distinctly different from *T. fetus*.

Recent studies have shown that it is highly probable that *Trichomonas suis* frequently found in the digestive

tract and nasal cavity of swine is similar to *T. fetus* based on morphology, clinical signs produced by injections of *T. suis* into the genital tract of heifers and on serologic tests.^{30,39,41,49-51} The fact that these two protozoa from different body sites in swine and cattle are apparently identical may well account for the spread of the disease from swine to cattle, especially beef cattle where the two species are often housed together.

In cattle, *T. fetus* is found only in the female genital tract, vagina, cervix, uterus, and uterine tubes, and on the penis and prepuce of the bull. In rare and unusual instances retrograde trichomonad infections of the seminal vesicles or epididymides may occur.^{12,16} The greatest concentration of organisms in the bull was found in the fornix, on the glans penis and adjacent prepuce.^{12,37}

Trichomoniasis is a venereal disease spread from animal to animal at the time of coitus or artificial insemination. Trichomoniasis may be spread from bull to bull in an AI stud at the time of semen collection or if bulls are allowed to run together and mount each other. Only rarely is it spread by other means such as by grooming animals that have a discharge from the vulva, or by the use of contaminated instruments, speculums or preputial or vaginal douching nozzles.¹² Placing many *T. fetus* organisms on the vulva of heifers failed to cause infection.²⁵ The transmission of trichomoniasis by artificial insemination was first reported in 1939.³³ By means of 7 inseminations, the disease was produced in 6 out of 9 uninfected females, and thus demonstrated that trichomoniasis could be spread by artificial insemination with fresh undiluted semen from an infected bull.^{7,12} Semen from an infected bull was diluted 1 to 25 to 1 to 80 times in an egg-yolk-citrate buffer with sulfanilamide.⁶⁶ Of 600 cows inseminated by semen from the infected bull 5 showed early abortion and 1 developed pyometra. Trichomonads were present in 7 out of 28 ejaculates collected from infected bulls. Storage of the liquid infected semen in the usual manner, and the addition of antibiotics and extenders apparently had little or no inhibitory effects on the organisms.⁴⁴ In 1953 examination of 168 bulls in 5 artificial insemination associations found 23 infected.¹³ The rate of transmission of infection by artificial insemination was estimated at less than 1 percent. This would not be serious in artificially inseminated cows and the percentage of conceptions on first service of infected bulls would not be noticeably affected.⁴⁶⁻⁴⁸ On the other hand in some herds bred artificially, the incidence of infection was as high as 20 percent.⁶³ The transmission rate might be serious, however, if the infected cows were bred to the herd sire and the disease thereby transmitted. The low incidence of infection from artificial insemination is due to the methods of

collection, storing, and dilution of the liquid semen. Only by the recovery of the organism in occasional isolated abortions or pyometra cases can trichomoniasis be traced to infected bulls used in artificial insemination. A high infection rate in nonimmune heifers when bred artificially with infected semen was reported even though the semen was extended 1 to 40.⁶⁶ A great difference between infected bulls in the ability of their semen to transmit infection when used for artificial insemination was noted. This may be due to the great difference in the number of organisms present in the sheaths of different bulls.¹² The previous evidence was reviewed and confirmed the fact that *T. fetus* could survive in frozen and thawed extended bull semen even though glycerol was toxic to *T. fetus*. In glycerol-egg yolk-citrate extender *T. fetus* did not survive freezing and thawing; while in glycerol-egg-yolk phosphate or glycerol-milk extenders some organisms did survive. Thus bulls used in AI service should be free of trichomoniasis or spread of the disease might rarely occur.⁴⁵

In natural service the transmission rate of the disease is about 80 percent. In 24 susceptible females bred to an infected bull, only 28 natural breedings were necessary to produce infection in all the females.^{7,9,12} After natural service to an infected bull 23 of 26 heifers became infected but the conception rate was 45 percent.⁶⁵ Of twenty heifers bred to an infected bull, 19 became infected after one service. From 15 to 50 days postservice organisms were found in all 8 slaughtered heifers in the vagina and cervix, in the uterus in three-quarters of the heifers and in the uterine tubes in one half of the heifers.⁵⁹ No gross or microscopic lesions were present in these heifers. In 12 heifers slaughtered between 60 and 100 days postservice, 7 had acute or chronic lesions in many areas of the genital tract, 2 of these had impending abortions and 1 had pyometra. The other 5 heifers of the 12 had no microscopic lesions and in only one of these was *T. fetus* recovered from the cervix and vagina.⁵⁹ In another transmission trial a noninfected bull bred an infected cow and then bred nonexposed cows within 20 minutes; 25 percent of the latter became infected. If the time between services was extended to 3 to 24 hours none became infected and all conceived. Thus noninfected bulls may passively transmit infection during mating but the rate of transmission is low.²⁵ Bulls were also quite susceptible to infection with 4 of 9 bulls becoming infected after the first service to an infected cow. However, 2 of 9 bulls proved highly resistant and could not be infected after 6 services to infected females. Young bulls with less well-developed mucosal crypts and folds in the prepuce are much more resistant to experimental infections than are older bulls. Bulls under four years of age are

seldom found naturally infected and are difficult to infect experimentally.² Exceptions to this observation may be due to breed or individual differences in susceptibility as a few 2 year-old infected bulls have been reported.^{1,52} Bulls, unlike cows, do not seem to be able to develop immunity, even after 2 or 3 infections. If given sexual rest for a period of time cows will usually develop an immunity and rid themselves of the infection; whereas once a bull becomes infected the infection is permanent and only occasionally does spontaneous recovery occur. Cows may readily be infected experimentally by the introduction of *T. fetus* into the vagina or uterus. Although bulls are less susceptible to artificial infection of the prepuce, they more readily contract trichomoniasis after natural service to an infected cow. Except in sporadic cases due to artificial insemination the disease usually appears in a herd as an insidious venereal enzootic infection.

Signs—Being insidious in nature, trichomoniasis is often well-established in a herd before the symptoms reach proportions sufficiently alarming so that a veterinarian is called. The breeding records of any herd affected with sterility should be carefully studied. The possibility of the presence of this disease can often be surmised on the basis of good breeding records. Often the original source of the infection can be traced to a certain bull or non-pregnant cow added to the herd. Purebred herds that sell breeding stock should be extremely cautious in accepting "returned" infertile animals back into their herd after they have been exposed to cattle in other herds.^{24a} Infertility frequently starts after such additions. Once the disease has been diagnosed, herd records are also of value in planning a control program. After the cows have been exposed by coitus to a trichomonad-infected bull the following signs may be observed:

(1) Trichomoniasis will fail to become established in a small number of cows or heifers either because of the small numbers of trichomonads introduced or because of the natural resistance of the female. Conception and a normal gestation period will follow. Approximately 5 to 20 percent of the cows or heifers may fall in this category. Normal gestation and parturition may result in spite of the infection.^{57,65} Trichomonads have been isolated on rare occasions throughout a gestation period terminating in a normal parturition.

(2) When *T. fetus* becomes established after coitus there is no reaction nor any clinical lesions or discharge for the first 3 or 4 days. However, by 4 to 9 days the presence of a moderate vulvovaginitis and cervicitis may be observed on clinical examination. Discharges from the genitals are absent or very scanty during most infections unless pyometra occurs and then a mucopurulent

exudate is usually discharged irregularly. Under field conditions these symptoms in most cattle would usually pass unnoticed.¹² The above symptoms are so slight as to be of little significance and other infections of a non-specific type may produce similar symptoms. In rare instances a more severe and chronic type of vaginitis may develop in the cranial portion of the vagina in cows with trichomoniasis. This is characterized by a rough, rasp-like corrugated vaginal mucosa. Some clinicians indicate that this lesion when observed is nearly pathognomic for the disease. Trichomonads may be found in the vaginal exudate, which is usually watery, clear, or cloudy, often containing whitish-yellow flakes of pus. The presence of trichomonads in a cyst of Gartner's duct 11 weeks after the apparent recovery of the cow from trichomoniasis was reported.¹⁵ In general, clinical symptoms are absent or mild and usually pass unnoticed by the herdsman.

The acutely or chronically-infected bull shows no gross lesions.

(3) The most common symptom of trichomoniasis is infertility, characterized by the necessity for many services per conception and by the frequent occurrence of a prolonged period between estrual periods after breeding. One herd of 50 cows during the height of the infection had an average of 5.15 services per conception over a 2-year period. Prior to the development of the disease the conception rate had been a normal 1.82 services per conception.^{7,9,10,12} Some cows must be bred 6 to 8 times before conception occurs. *T. fetus* produces a mild inflammation of the uterine tubal epithelium, endometrium, cervical and vaginal mucous membranes, and affects the developing embryo and fetus. There is no evidence to show that it may interfere with fertilization of the ova. Nearly 40 percent of infected cows after breeding showed shorter- or longer-than-normal inter-estrual periods during the time they were infected.¹² The longer interval between estrums were most commonly noted. Most of the trichomonad abortions or resorptions are caused by the early death of the embryo and fetus from 15 to 80 days of gestation rather than the less common and often observable abortions occurring after three months of gestation. In early embryonic deaths the embryos usually macerate and are absorbed in the uterus or are expelled unnoticed. Occasionally pyometra may result from a macerating embryo and the accompanying endometritis. If cows are infected at one service to an infected bull and fail to conceive, a subsequent service to a clean bull, either naturally or artificially, will not result in a safe conception until the cow develops an immunity and eliminates the organism. Thus infertility produced by the original infected bull persists even though subsequent breedings are to a noninfected bull. Tricho-

moniasis is actually characterized mainly by infertility and only occasionally by observable abortions and pyometra.

(4) Abortions due to *T. fetus* usually occur between 1 and 16 weeks of pregnancy.⁵⁷ Abortions occurring after 5 months of pregnancy are very rare. If an exposed cow has conceived and carried a normal fetus for 6 months, abortion due to trichomoniasis will probably not occur. Most fetuses aborted before 90 days are not observed. Those aborted the third to fifth month of gestation are usually slightly macerated and autolyzed and are expelled with the fetal membranes around the fetus along with a variable amount of dark, reddish-brown exudate. Occasionally on routine rectal examinations in infected herds these dead fetuses may be diagnosed. Retained placenta is very seldom observed following a trichomonad abortion. The number of observed abortions will vary in an outbreak, depending upon the severity of the infection, the closeness with which the cows are observed, and whether the outbreak is during the summer pasture season or during the winter months when the cows are stabled. Occasionally a mucopurulent reddish-brown discharge may precede an abortion. In a careful study of 50 infected cows, only 2 abortions were recognized and 5 cows developed pyometra.^{7,9,10,12} In 5 herds studied in Maryland involving 300 beef and dairy cattle, only 1 abortion and 1 pyometra were observed. In an outbreak involving about 20 cattle which the author was able to study and follow closely, 1 cow aborted a recognizable fetus and 1 had pyometra. An outbreak in a herd of 75 animals was cited^{21,22} in which 9 observed abortions and 7 unobserved abortions occurred in cows previously diagnosed pregnant. No cases of pyometra were noted. More often the history in an outbreak of trichomoniasis is that the herdsman believed a cow safely pregnant and then 60 to 90 days or more after service, estrus is again exhibited.

(5) Pyometra may be present in 0 to 10 percent of the cows in an outbreak of trichomoniasis. Trichomonad pyometra is postcoital or postservice and not postpartum. When death of the developing embryo or early fetus occurs and abortion or maceration and absorption do not occur, pyometra develops. The corpus luteum in the ovary persists and the cervix may remain tightly closed and sealed with no discharge of pus. More often, however, the cervical seal breaks down and a slight amount of pus escapes into the vagina and is discharged occasionally from the vulva. Since estrus does not occur with pyometra this condition may pass unnoticed for up to 8 or 9 months unless a vaginal discharge is observed or a diagnosis is made on rectal examination. The amount of pus in the uterus varies from about 60 to 8000 ml. with

an average of 1500 ml.⁵⁸ The pus in trichomonad pyometra has a characteristic thin, yellow-grey, watery, flocculent consistency, often containing yellow flakes of pus and shreds of fetal membranes and tissues; in rare cases small fetal bones may be present. The pus has been described as having a "potato soup" color and consistency. Odor may be absent or rather sweetish, but is not fetid. No evidence of perimetritis or other uterine lesions are present. If on rectal examination a diagnosis of pyometra cannot be made positively, another examination 1 or 2 months later is indicated. Usually trichomonads may be recovered in pure culture from this pus. In examining 20 cases of trichomonad pyometra trichomonads were found in every case in numbers from 320 to 3,520 million per ml. with an average of 1552 million per ml.⁵⁸

Diagnosis—The history of the introduction of a new infected animal into a herd followed by a gradually increasing problem of infertility characterized by failure of conception after frequent services, prolonged periods after service before the next estrual period including cows apparently conceiving but coming into estrus several months later, and the occurrence of occasional early abortions and pyometra are characteristic symptoms of this disease. In recently infected herds all cows and heifers are susceptible. In more chronically infected herds most cows have an acquired immunity, while virgin heifers are susceptible. These symptoms are also quite characteristic of vibriosis due to *Campylobacter fetus venerealis*. Some bulls are infected with both vibriosis and trichomoniasis. The positive diagnosis of trichomoniasis, as in vibriosis, requires the finding of the organism in one or more infected animals or a diagnosis based on immunologic reactions due to the local immunity developed in the genital tract.

Diagnosis in the bull consists of checking the natural breeding records and finding which older bulls are probably chronically infected and checking the preputial smegma of these particular animals carefully, and if necessary repeatedly, by the swab, the pipette, or the douche method. These older bulls are of great diagnostic value for detecting the presence of *T. fetus* infection in a herd.² After natural service the numbers of organisms on the penis and sheath are reduced. Following a period of sexual rest for 5 to 10 days to allow the numbers of organisms to increase, the bull is confined in a stall, chute or stanchion. A sideline on the bull is often helpful in restraining the animal in a stall. To avoid fecal or other contamination from the preputial hairs, they are clipped and the preputial orifice is thoroughly washed with soap and water, rinsed, and wiped dry. After its head is fastened and its tail pushed up and forward as restraint, the

abdomen is stroked and then the sample is taken from the prepuce. This sampling procedure can be hazardous to the operator because all range bulls and most dairy bulls resent this sampling and will kick violently unless they are accustomed to being handled and groomed. The use of a bull electroejaculator may be helpful in diverting the bull's attention and getting him to stand quietly.^{56b}

For direct examination of the preputial smegma for the presence of *T. fetus*, the swab, the pipette or the douche method may be used. In the swab technique, a sterile cotton swab or one made with one-half of a 4 × 4 gauze pad soaked in a physiological saline or lactated Ringer's solution is introduced into the sheath on a 36 to 40 inch wire or long narrow forceps, or wrapped around the bristles of a small brush on the end of a long wire. The sheath is swabbed in a back-and-forth circular motion in the region of the fornix and glans penis where most of the trichomonads are located. The swab is then removed and placed in a small amount of physiological saline solution. This may be examined at once on the farm or later in the laboratory. The pipette technique^{1,2,10,12} consists of introducing a 24-inch sterile, Bartlett, plastic preputial or plastic Al pipette with attached bulb or syringe from which the air has been expelled. In the average adult bull which has not been used for service in several days, 1 to 10 ml. or more of smegma and fluid may be removed by aspiration from the sheath by a back-and-forth gentle scraping motion of the end of the pipette in the region of the glans penis. This is flushed into a vial containing 5 ml. of physiological saline, lactated Ringer's solution or Kupferberg broth⁴⁸ refrigerated and examined later in the laboratory. The douche technique consists of introducing 200 to 250 ml. of sterile physiological saline into the sheath and closing the external orifice with the fingers to prevent the loss of the saline solution.^{17,29,37} The solution is vigorously massaged back and forth in the sheath for several minutes and allowed to run back out of the sheath into a broad-mouthed beaker and poured back into a bottle for laboratory examination. Occasionally this procedure will stimulate the bull to urinate and require the douching to be repeated.

Since the *T. fetus* organisms often occur in the infected bull in small numbers they must be located in fresh samples in which the organism is alive and motile or cultured to increase the number of organisms. The combination of the pipette technique with culturing is about 95 percent accurate.¹ Samples must therefore be handled properly after collection, by avoiding extremes of temperature, contact with harmful chemicals, and evaporation. It is highly desirable to examine samples or culture them within a few hours of collection. If an immediate examination is not possible the samples may be kept in

a cool place such as a refrigerator or shipped to a laboratory under refrigeration to control bacterial growth, and examined within 24 to 48 hours. Ordinary freezing at 32° F. will destroy trichomonads. Pipette samples should be allowed to settle for several hours or centrifuged for 10 minutes at 2000 R.P.M. After most of the supernatant fluid is poured off, the superficial layer and the sediment where the organisms are concentrated are mixed. This material is dropped on a glass slide to make a thin pool that is examined under low power with a reduced amount of light. A cover glass should not be used; 3 slides must be carefully examined before the sample is considered negative. A similar technique is used in examining swabs. In the douche technique, the 250 ml. of saline solution and preputial washings are centrifuged for 10 minutes at 2000 R.P.M. at the laboratory. [If a large centrifuge is not available allow the preputial washings to settle for one-half hour and draw off 15 ml. of the sediment and centrifuge the latter. Take a small amount from the bottom of the tube and examine on a warm slide under subdued light for the presence of trichomoniasis.^{24a}] After the supernatant fluid is decanted, the remaining material is centrifuged in a like manner in a 15 ml. centrifuge tube. The supernatant fluid is poured off and the sediment is mixed with 0.5 to 1 ml. of the remaining fluid and examined. The pipette method was superior to the swab technique, and the douche technique superior to both.²⁹ In the field where a laboratory was not available the swab and pipette methods were most practical. Using the pipette technique a positive test was recorded on 42 to 85 percent of the samples from known infected bulls.¹³ Two infected bulls were considered atypical inasmuch as only 8.5 to 19.5 percent of the preputial samples from them were positive. Of 23 infected bulls of 168 bulls examined, 15 were diagnosed on the first sampling, 6 on the second and 2 on the third sampling. In rare instances positive bulls may not be found until the fifth sampling with the pipette; for this reason these workers recommended that at least 6 negative samples at weekly intervals be considered as a minimal diagnostic routine under practical conditions. The use of the more cumbersome douche technique might reduce the numbers of preputial samples required. The direct swabbing or scrubbing of the exposed glans penis with gauge sponges in saline solution appeared promising in detecting infected bulls when the numbers of trichomonads present were low. The penis was exposed manually after tranquilization of the bull. Semen examinations for trichomonads are not feasible since sperm motility interferes with the examination.

By the use of modified Plastringe or Diamond's or other media containing nutrients and antibiotics, prepu-

tial smegma material can be layered on culture media and incubated for 3 to 5 days and examined.^{1,3,35,43,48a}

This method utilizes the collection techniques outlined above and the modified douche technique for obtaining a sample of smegma. The smegma or mucus for culture when placed on top of the media allows the motile anaerobic *Trichomonads* to migrate to the bottom of the culture tube while the contaminating bacteria remain at the top of the tube. The inoculated tube is incubated at 38° C and the fluid at the bottom of the tube is pipetted out and examined in 24 and 48 hours for trichomonads. Culture techniques save a great deal of time when compared to the direct microscopic examination by a skilled person. It is also a more accurate technique.

Diagnosis in the cow may be accomplished by examination of the aborted fetal membranes, the mouth cavity of the fetus, the fetal fluids, the stomach contents of the fetus, or the exudate in the uterus for *T. fetus*. Following abortion the organisms usually disappear within 48 hours. In cows with postcoital pyometra the exudate should always be examined for trichomonads. *T. fetus* are often found in such great numbers that dilution is necessary in order to observe them clearly. In cows bred artificially, early abortion and pyometra are about the only conditions in which trichomonads might be found or suspected. The early occurrence of vaginal immunity to the organism is responsible for the disappearance of trichomonads from the vagina. The organism which is motile traverses the cervix into the uterus where it remains and produces an endometritis that lasts for one to several months. During this time organisms may be found periodically in the vagina. Vaginal samples from suspected females should be examined during the early vaginal phase of the infection, which lasts for about 5 weeks after the coitus that produced the initial infection. Thereafter the presence of vaginal infection may occasionally be observed about 3 to 7 days before estrum.³⁸ This pattern occurs only in previously uninfected animals. Consequently in selecting females to culture it is best to select if possible virgin heifers bred the first time to a supposedly infected or suspect bull. Sample the vaginal mucus with a 14- to 16-inch-long, plastic pipette in a manner similar to the examination of the bull. These samplings should be made 12 to 19 days after the infecting service and then 3 to 7 days prior to each subsequent estrum. In one trial only 7 of 36 cows bred to infected bulls had positive cervical-vaginal mucus cultures about 90 to 100 days after service. Seven of the 36 cows, 2 percent, aborted but only 3 of these, or 8 percent of the 36 cows had positive cultures.³ Finding the trichomonad organisms in cows cannot be done as regularly nor as easily as in bulls so the cow is less fre-

quently employed for routine diagnostic purposes.^{2,3}

It may be desirable to check certain bulls further and for this purpose 2 or more virgin heifers may be bred naturally and vaginal samples taken regularly from 12 to 19 days later. If no positive recoveries of the organism are made, the bull may tentatively be considered free of the infection. Vaginal exudate, if present, should be taken from any suspected cow and especially from cows exhibiting a rough, rasplike corrugated vagina and examined for *T. fetus*.

The living *Tritrichomonas fetus* can be readily identified under the microscope by its characteristic size, shape, undulating membrane, and jerky, erratic motion and continuous rolling.⁵² *T. fetus* in live culture seldom if ever ceases to move, whereas other protozoa occasionally stop moving. Other protozoa, such as: *T. ruminatum*, *Entrichomastix ruminatum*, *Bodo fetus* and others, may also be observed, especially in contaminated samples containing feces.⁵⁷ Their size and motion however, differs from that of *T. fetus* and they have no undulating membrane. These other forms of protozoa are more likely to be observed if samples are held for 18 to 48 hours at room temperature before examination or if samples are taken from the cranial portion of the prepuce.

In pregnancies that terminate in abortions at 90 to 150 days or in pyometra, *T. fetus* may survive for 4 to 5 months in the genital tract of a cow. In most cows however the infection may persist for only a few weeks, 4 to 5, in the vagina and for up to about 60 to 90 days, 2 to 3 months, in the uterus before local immunity results in spontaneous recovery. Infected bulls may remain as carriers of *T. fetus* but no lesions or inflammation of the sheath or penis is produced in either acutely or chronically infected males.

A vaginal mucus agglutination test has been described.⁴⁹⁻⁵¹ Since agglutinating antibodies are developed locally in both the vagina and uterus this has been used as a herd test for *T. fetus* infection. It is not satisfactory for testing individual animals. The antibodies appear as early as 18 to 21 days after infection but reach a high level by 40 days. No systemic antibodies with blood titers were ever observed. In northern Ireland this test was used as a herd screening test to locate those herds that were infected.

Prognosis—The prognosis is usually good if the owner follows a carefully planned control program. In the individual cow the prognosis is good because the non-pregnant cow tends to develop an immunity which although temporary, eliminates the infection in about 3 to 6 months. However the immunity produced is relatively short-lived and reinfection may occur.^{1,2} In certain cases

of uterine infection in pregnant cows, or of pyometra, the infection may survive in the uterus for much longer periods or until abortion or parturition occurs or the pyometra is cured. Occasionally secondary invading organisms such as *C. pyogenes* may produce a more severe pyometra and sterility. Cows very rarely, if ever, carry *T. fetus* infection in their uterus through an entire gestation period. In some longstanding cases of infertility due to pyometra or chronic endometritis, conception may fail to occur and the cow is sold for economic reasons. The prognosis for bulls is more guarded. Since older bulls are usually permanently infected and only very rarely recover spontaneously they usually are sold for slaughter unless they are valuable and treatment is decided upon. Any bull not worth more than 3 times his salvage value should be slaughtered. If the bull is valuable then treatment and posttreatment testing involving a period of about 3 to 4 months is indicated. Treatment and the many post-treatment test samples required are expensive. Fortunately treatment is highly effective.⁶³

Herd treatment—The various possible programs that can be used to eliminate the infection should be carefully explained to the herdsman and the owner. The veterinarian can usually outline a practical plan or procedure for the control of trichomoniasis in the herd. There is no satisfactory or successful method to immunize cows artificially against trichomoniasis.

The most practical and easy method to control and eliminate trichomoniasis in a dairy herd is stop all natural service and breed all cows having normal genital tracts by artificial insemination to disease-free bulls for a period of about one to two years before resorting again to natural service by bulls proven free of *T. fetus*, or by virgin bulls. Cows with pyometra should be treated and cows that abort or have an embryonic resorption should not be rebred for 1 or 2 months after the uterus involutes to its normal state. If artificial insemination is utilized for all cows, this author sees no benefit from requiring that all cows have 3 normal length cycles prior to re-breeding to ensure that most cows will have freed themselves of the infection. This may promote a higher rate of conception on first service but the loss of production would be excessive by such a delay in service on many cows in the herd that may be nearly recovered or have recovered from *T. fetus* infection. However the owner should be warned that an increased number of services will be necessary, especially on cows that had been recently infected and have not developed an immunity. Infected bulls should be sold or, if valuable enough, should be treated. Breeding infected bulls to supposedly immune cows may result in fairly satisfactory conception rates but the infection will continue in the herd. Im-

munity to trichomoniasis lasts only a short period of months. Even cows that have conceived and had a normal gestation period and parturition should not be bred back by natural service within 90 days of calving, since cows may rarely carry the infection through the gestation period. Infected and noninfected cows may be housed or pastured together with practically no danger of spread of the disease since trichomoniasis is rarely spread except by venereal contact. This above practical artificial insemination procedure will work well for most dairy and a few beef herds, if no bulls are kept and if close veterinary supervision and good management are available.

Another control method that is rather difficult to carry out is to divide the herd of female cattle into two groups

(1) the clean nonexposed cows and heifers including virgin unbred heifers, pregnant or open heifers or cows that have never been bred by a known trichomonad-infected bull or a bull suspected of being infected and nonpregnant cows that have recently calved after a normal gestation period and have not had a service by an infected or suspect bull. Any cow or heifer where the breeding history is not definitely known should be placed in the second "infected" group.

(2) the infected or possibly infected cows or heifers include those pregnant or nonpregnant animals that have had coitus with an infected or suspect bull and have not had a normal gestation period following that service.

In Group 1 the noninfected cows and heifers may be bred by a noninfected or virgin bull or by artificial insemination. In Group 2 the "infected" or "suspect" nonpregnant females should be given 60 to 90 days, or 3 normal estrous cycles, sexual rest before being rebred to cheap noninfected "sacrifice" bulls which can be slaughtered at the end of the breeding season. All pregnant and nonpregnant cows should be examined at monthly or bi-monthly intervals until they are pregnant 6 months or more, or are sold as infertile. Females with pyometra, abortions or metritis should be treated before breeding or sold for slaughter. After calving these cows should not be rebred for a period of 60 to 90 days and then they may be bred naturally to a noninfected bull. This latter method has been employed successfully in a number of beef herds where the "infected" and "noninfected" herds can be kept some distance apart with no danger of contact or mixing of animals between the two herds. In a few beef herds the disease was eradicated by breeding virgin bulls to virgin heifers and keeping these animals together and separate from the infected herd for a number of years until the infected herd could be eliminated or replaced. Accurate breeding records, carefully identified cows and bulls, good fences and intelligent man-

agement is necessary to eliminate this disease by methods other than by selling all bulls and going into an artificial breeding program for all the females in the herd.

Individual treatment—The treatment of most infected cows is not necessary, inasmuch as these animals if given sexual rest will overcome the infection. Cases of pyometra and abortion and secondary metritis must be treated and handled as described later in this chapter. Many veterinarians feel that with treatment, recovery may be more rapid and complete. To satisfy the owner that something is being done for these heifers or cows, many of which have been bred repeatedly, treatment is often undertaken. These treatments which are of questionable value may include douching of the vagina and possibly the uterus with 2 to 3 ml. of Lugol's solution in 100 ml. of water, 4 to 5 percent sodium perborate solution, 1 to 3 percent chlorine solution, or 1 percent acriflavine solution, once or at several intervals a week or 10 days apart. Various antiseptic treatments of the genital tract of the infected cow were useless in elimination of the organisms, which can be done only by the development of immunity.⁶⁵ Some veterinarians will sample and culture the cervical and vaginal mucus or uterine exudate in pyometra. If infection is present they will treat the cows orally or parenterally with drugs recommended for the treatment of bulls.

Treatment for bulls has received much attention in the last 30 years. For the first 20 years a number of different techniques and drugs were used to affect a cure mainly by local treatment of the prepuce and penis, often at repeated intervals that was very time-consuming and expensive. These treatments of "Bovoflavin Ointment," acriflavine ointment and hydrogen peroxide and others used locally and sodium iodide intravenously or their combination has been described.⁶⁰ These treatments are presently seldom used because of the difficulty or dangers in their application and the not uncommon failures in the cure of the *T. fetus* infection.

Presently the treatment of choice is the oral administration of 50 mg/kg or 25 mg/lb of body weight of dimetridazole (1,2-dimethyl-5 nitroimidazole) (Rhodia Inc. N.Y.C. or Emtryl, Salisbury Laboratories, Charles City, Iowa). This drug is used for the treatment of blackhead in turkeys and like the following drug is not approved in cattle.^{1,24,52,54-56} Another similar drug metronidazole (1-B-hydroxyethyl-2-methyl-5-nitroimidazole (Searle, Chicago, Ill.) is used for treating *T. vaginalis* in humans.^{1,34} The dose of this latter drug was 10 to 75 mg/kg of body weight intravenously every 12 hours for 3 injections or once daily for 2 days. Dimetridazole can also be given intravenously in a 10 to 20 percent sulfuric acid solution at a dose level of 10 mg/kg of body weight daily for 5 days or 50 to 100 mg/kg of body weight at

a single injection. Because of severe side-effects of dyspnea, ataxia, recumbency and weakness from intravenous therapy the oral therapy is preferred. Dimetridazole is usually administered by boluses, drench or by stomach tube. When mixed with feed it may be unpalatable so it may not be completely consumed. Since bulls on a high concentrate ration may develop rumen stasis, a ration high in roughage should be fed before and during treatment. Following therapy a designation of a cure should be based on 3 consecutive negative cultures over a period of six weeks starting 45 to 60 days after treatment.⁵² The possibility of strains of *T. fetus* developing resistance to dimetridazole has been reported.⁵⁵ Dimetridazole has been used at the dose level of 25 mg/lb daily for 5 days orally to treat over 100 bulls with trichomoniasis with 90 to 95 percent success in eliminating the infection.^{24a} It is doubtful that any commercial company will for economic reasons go to the expense of obtaining official approval of dimetridazole for the treatment of trichomoniasis in bulls and cows. Preliminary evidence indicates the drug may be present in milk from treated cows for a period of 4 to 6 days.^{24a,b}

Treatment of bulls without eradication of *Trichomonas fetus* in the herd is useless, since bulls which have recovered are susceptible to reinfection. Careful observation and repeated checking of the bulls after treatment is necessary. This is the most important aspect of the treatment of bulls for trichomoniasis. For 3 months after treatment with Bovoflavin Ointment negative preputial samples even if collected twice a week have little significance. Furthermore, test matings with susceptible females were not reliable during this period. Coitus with 2 or more virgin heifers might be allowed at intervals during this posttreatment period and vaginal mucus samples should be examined and cultured frequently between 12 and 19 days after coitus. If still negative the bull can be restored to service but careful observations should be made on females bred to him.

Further studies on cure rates and the required testing protocol to be followed in assessing the posttreatment status of bulls after the use of the nitroimidazole drugs is indicated.

Prevention—Preventing the introduction of trichomoniasis into a herd is of vital interest to an owner and his veterinarian. The precautions should include: knowledge of the reproductive efficiency in the herd of origin of any stock purchases; thorough examination of newly-purchased suspect bulls with a pipette to obtain preputial samples for culture, at least 3 to 6 times at weekly intervals; repeated examinations 12 to 19 days after coitus of the vaginal mucus of the first 3 or 4 cows and heifers bred to these bulls; and prohibition of coitus for newly-

purchased nonvirgin, nonpregnant heifers and nonpregnant cows that have had coitus since their last calving, to prevent the introduction of trichomoniasis by females. These animals should be bred by artificial insemination. All recently acquired cows that are pregnant should be withheld from coitus for 90 days after calving and allowed to pass at least 2 heat periods before being bred naturally.¹²

In artificial breeding centers the need for a careful examination and history on the bulls before purchase, and proper and frequent examination, 3 to 6 negative preputial examinations at weekly intervals, of all service-age bulls as they enter the stud and periodically thereafter is essential to prevent the possible introduction and spread of this infection into many herds. Owners should be careful of their source of semen for artificial insemination in their herds especially if a herd sire is also maintained.

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VIBRIOSIS

Definition—Vibriosis or venereal campylobacteriosis is a venereal disease of cattle caused by *Campylobacter fetus venerealis* spread at the time of coitus or at the time of artificial insemination with improperly handled and treated semen, and characterized by infertility with an increased number of services per conception. Early embryonic deaths are common and abortions from 4 to 7 months of gestation are occasionally observed. The cow develops an immunity to the infection and will have a subsequent normal gestation period but may remain a carrier for many months. The older bull remains a chronic carrier of infection. Although the name of the organism has been changed from *Vibrio* to *Campylobacter* the disease will continue to be called Vibriosis.²⁴

Etiology—Vibriosis was first described in 1910 and 1913 in sheep and cattle. During the period of 1918 to 1923 a number of reports were made on the causative agent, pathogenesis, and other factors associated with this disease^{68,69,70} and the organism called *Vibrio fetus* now called *C. fetus*. This organism may appear as motile, or nonmotile, gram-negative, short, comma-shaped rods, or as double spiral-shaped filaments. It grows slowly, scantily, and with difficulty on most laboratory media. All laboratory animals except guinea pigs appear refractory to infection but the organism may be pathogenic for chick embryos. *C. fetus*, is pathogenic for man in which it causes an undulating fever, placental infection and abortion.^{25,26} There is a close genetic relationship between certain ovine, bovine and human vibrios

so human vibriosis might be acquired by contact with animals.

Within the past 25 years the various pathogenic vibrio have been isolated and studied.^{8,18,19,24,50,80} (See Table 18.) *C. fetus venerealis* is a serologically homogenous strain and both Type I and Subtype I (or Type II)^{27-29,50} are similar in antigenicity and pathogenicity. *C. fetus intestinalis* is also pathogenic in that it is a common cause of abortion in sheep and causes sporadic abortions in cattle. *C. fetus intestinalis* only rarely produces infertility.¹⁹ It can survive for a period of time in the gut of animals but does not persist in the genital tract of cows. There are 3 serotypes of *C. fetus intestinalis*; A and B are found in the intestine of sheep and cattle while C, including *C. fetus jejuni*, are found in the intestines of mammals and birds. This latter serotype C causes abortion in sheep and enteritis in dogs and man.²⁴ *C. bubulus* also found in the genital tract does not produce disease and²⁴ does not persist in the genital tract of cows. *C. bubulus* is a nonpathogenic vibrio that is commonly found in fecal material and in the cranial portion of the prepuce of bulls.

C. fetus venerealis is an obligate parasite found only in the female genital tract and its contents, fetus and placenta, and in the prepuce of the bull. *C. fetus venerealis* localizes in the anterior vagina and cervix and usually invades the uterus about 7 days after natural service to an infected bull. The infection remains in the uterus and oviducts for a number of weeks to 3 months producing a moderate endometritis and salpingitis.^{24,64} This results in infertility and early embryonic or fetal deaths. When an immunity develops the infection is eliminated. However, the infection may remain in the cervix and vagina for 8 to 18 months or more. Rarely a cow may carry the infection through a normal gestation period.^{19,22,53,58,59} Vulvar exposure of susceptible heifers with *C. fetus* failed to produce infection so spread of the disease by contact is unlikely.⁴⁷ Young bulls under 4 or 5 years of age are difficult to infect. They may carry the organism from cow to cow during the breeding season but rapidly become free of infection when isolated from infected cows.

In bulls over 5 years of age vibriosis may become a chronic infection in the prepuce and persist for years. The numbers of vibrio organisms in the sheaths of infected bulls varies greatly. Most of the organisms are present in the deeper portions of the sheath around the glans penis and fornix but no lesions are produced.^{21,28,63,77} Thus the carrier female as well as the carrier bull are responsible for maintaining the infection in the herd from year to year. Under certain circumstances bulls may develop immunity. The immunity or resistance in cows is not a strong one but is sufficient in most cases to permit conception and a normal gestation even if the organisms survive in the tract for several days or weeks.^{31,32,34,35}

C. fetus venerealis from the prepuce contaminates the semen as the organism has never been found in the deeper portions of the male reproductive tract. Special media, techniques and experience are required for the laboratory recovery of *C. fetus venerealis* from mucus from the vagina, cervix and uterus of cows and especially the contaminated mucus of the bull's prepuce. The Campylobacter organism is highly susceptible to light, drying and other adverse influences. It cannot live in the alimentary tract of the cow.⁸

Vibriosis is a venereal disease of cattle spread by the chronically-infected bull to susceptible cows by either natural or artificial service. The initial studies on this disease were done in the early 1950s.^{41,45,46,71,75} *C. fetus venerealis* was probably the most important cause of infertility in beef cattle in the western range states until preventive vaccines were commercially available.^{28,29,36,79} It may still produce significant infertility and losses in range beef herds. Until the advent of the widespread use of artificial insemination with antibiotic treated semen it was also a very common cause of infertility in dairy herds in the U.S.A.

Vibriosis has been reported widespread in nearly every state in the United States, in Australia, South Africa, Sweden, England, Holland, Canada, and other countries in the world. The presence of *C. fetus* in the semen can be explained in the same manner as the presence of

Table 18. Cultural Characteristics of the Common Campylobacter Organisms

Vibrios	Catalase	H ₂ S Production	Tolerance to 3.5% NaCl	Tolerance to 1% glycine	Fluorescent Antibody Reaction*
<i>C. fetus venerealis</i> (Type I & Subtype I)	+	—	—	—	+++
<i>C. fetus intestinalis</i>	+	+	—	+	(+)
<i>C. bubulus</i>	—	+++	+	+	—

*Conguate prepared from *C. fetus venerealis* (Obtainable from Armour-Baldwin Lab.).

trichomonads in the semen, namely by contamination of the artificial vagina at the time of service. **C. fetus** infections were found in 25 of 45 herds investigated in the region of Beltsville, Maryland.^{20,21} A 38 percent incidence of vibriosis infection in beef herds in California was reported based on the mucus agglutination test.³⁹ These herds had histories that were suspicious of vibriosis. Sixty percent of the 105 herds in Sweden studied by means of the mucus agglutination test were, or showed evidence of having been, infected with vibriosis.⁶ Thus vibriosis is probably much more widespread and common than is trichomoniasis and for this reason is of greater economic importance. Although abortion has been produced in a few animals by the intravenous injection of the organism, introduction of organisms into the animal's body by any means other than the genital tract of the female or the prepuce of the male has not resulted in infection. It is probable that natural infection of the cow except by coitus or artificial insemination is rare. Occasionally the infection might be spread from cow to cow by improperly cleaned instruments or insanitary procedures used in the treatment of the genital tract of cows. Infection except by coitus or insemination rarely if ever occurs even when infected and noninfected animals run together.^{21,41,46} In artificial insemination studs there is definite evidence of the intrastud spread of infection. Of 143 bulls in an artificial breeding stud 56 percent were infected; the percentage of infected animals was the same for 39 bulls that had never had a natural service as it was for 104 bulls that had previously been in natural service.³⁸ It was felt that contact and spread of infection between clean and infected bulls occurred on teaser bulls or steers at the time of semen collection or in pens where a number of bulls ran together and mounted each other. Over 20 percent of all bulls used artificially in Denmark were infected with **C. fetus**.^{60,61} The incidence of infection in susceptible cows is high following coitus with infected bulls. For example, of 30 virgin heifers bred with infected fresh semen at a dilution rate of 1 to 4 with extender without antibiotics, 26 heifers developed vibriosis.³⁸ Prior to the addition, of antibiotics to semen, artificial insemination was probably a major factor in the spread of this disease.⁶⁰ It is significant that in one large AI organization that conception rates based on 60 to 90 day nonreturns rose from 52 percent in May of 1948 to 74 percent in September of 1949 after the addition of antibiotics to the semen. No other changes or treatments were made in the semen collection, processing, or insemination. Since the advent of the regular and proper addition of antibiotics to semen the incidence of the disease is practically limited to herds using natural service. As with trichomoniasis the disease

is more prevalent in dealer's herds, valuable purebred herds, and institution herds, where there is a higher incidence of purchase and sale of cows and bulls. Virgin heifers and virgin bulls are free of the infection.

Signs—Vibriosis like trichomoniasis, is insidious in the manner in which it enters a herd. The condition may not be recognized for several months or more, until signs of infertility with failure of conception occur in a large number of cows. Herd infections have been described in the following manner.^{6,10b,21,41} **The acute type** of infertility problem is seen when the infection is first introduced by an infected bull into a susceptible herd. The drop in conception rate is marked, occasionally to less than 10 percent and the infertility may last for 2 to 6 months or more. Within this time the cows usually develop immunity with the production of antibodies of the IgA class that persist for months in the vagina. While the IgG antibodies are found in the uterus and rid that organ of infection in the convalescent phase of the disease,^{13,24} a cell mediated immunity may also be involved.¹³ Conception will follow breeding to either an infected or noninfected bull. Prior to the development of this immunity, breeding to a noninfected bull or with noninfected semen does not correct the infertility as the **C. fetus** organisms are present in the female from the original infecting service. **The chronic or subacute type** of infertility in a herd may be characterized by a history of an acute fertility problem in the past. Only a vague or intermittent infertility is present in the cows or in newly-purchased cows but a considerable amount of infertility may be present in the heifers after being bred to older infected bulls. This may not occur until the second breeding period if it is a practice to breed the virgin heifers in a herd to a virgin noninfected bull. In some herds the infertility may be limited to the portion of a herd served by a single bull, or it may involve all cows bred naturally, while cows being bred artificially with antibiotic-treated semen conceive normally. Examination of the bull and its semen usually reveals no abnormalities or lesions or explanation for the infertility. Abortions may occur in both the acutely or chronically affected herds but are more frequent in the acute outbreaks. Some virgin heifers have a natural immunity or develop it promptly and conceive within 2 months. Others conceive promptly but remain carriers of the organism for months. While others remain infected for months, have many services, or abort.^{58,59}

The specific signs of vibriosis in cattle may be listed as follows:

(1) Vibriosis may fail to become established in a susceptible animal after coitus with an infected bull, either due to natural resistance or because the numbers of or-

ganisms were too small to cause infection. Conception and normal gestation may occur. Occasionally the infection fails to establish itself rapidly in the uterus and cause the early death of the young embryo. Gestation therefore may continue for a number of months and then terminate in 3 to 7 months in abortion. The number of susceptible animals bred to an infected bull that fail to become infected are small, probably less than 5 to 25 percent. Thirty heifers that were artificially infected at the time of insemination; 7 conceived on first service and in 24 the infection became established.³⁸

(2) Endometritis and occasionally salpingitis has been described in *C. fetus* infection of the genital tract of cows and heifers.^{41,46,75} No vaginitis or cervicitis or other lesions were noted.^{28,53} A slight mucopurulent exudate may be present in the vagina. This may occasionally be noted as a discharge from the vulva and probably comes from the uterus or is due to other secondary infections. The infection or inflammation produced by *C. fetus* is mild in its effect on the mucosa. The estrual mucus may be cloudy and increased in amount in recently-infected heifers. The cervix may be reddened and postmortem gross and histologic examination of the uterus and endometrial biopsy may reveal an exudate and a slight to moderate degree of endometritis. By 30 days after inoculation of the cervix a subacute diffuse muco-purulent endometritis with a periglandular lymphocytic infiltration was present. The pathogenesis of *C. fetus* infection in cattle has been described.¹⁴ As the cow develops immunity and overcomes the infection, the estrual mucus becomes clear before pregnancy is established. In most recently infected animals the symptoms of endometritis pass unnoticed by the average owner or herdsman or are not detectable clinically. If cows are examined for failure of conception or infertility no specific signs of vibriosis can be observed. Rectal examination of the uterus is of no value in the diagnosis of an endometritis since the inflammation is so mild no obvious uterine changes are produced. No physical symptoms or lesions have been observed in the recently-infected bull. Most infertile *C. fetus*-infected cattle conceive before the endometritis and the organisms have completely disappeared.^{13,28,30}

(3) Infertility or failure of conception lasting for a period of 2 to 6 months, and in some herds 12 months, in susceptible cows or heifers bred naturally to an infected bull or bred artificially with fresh or frozen semen to which no antibiotic has been added is the most common symptom of vibriosis. Before 1950, it was thought that *C. fetus* was characterized principally by abortion; since 1950, however, infertility due apparently to the early death of the embryo caused by the *C. fetus* organism has been shown to result in the greatest economic loss. This

symptom of infertility and failure of conception, as in trichomoniasis, is the most constant and severe condition encountered with vibriosis. This has been demonstrated by field observations.^{21,41} In experimentally infected animals 19 artificially infected heifers required from 1 to 16 services, with an average of 5, per recognizable pregnancy.⁴⁵ In a similar experiment 20 heifers were infected.⁴¹ They required an average of 5.1 services per conception compared with an average of 1.3 to 1.6 services per conception for control heifers bred to uninfected bulls. A herd using 5 bulls, 1 of which was infected with *C. fetus* was described.^{20,21} The cows bred to the 4 noninfected bulls conceived with an average of 1.1 to 1.8 services per conception with 2.5 to 32 as the average number of days lost from first service to pregnancy. Of 18 cows bred to the infected bull, 5 failed to develop any infection and all 5 conceived on first service while the other 13 became infected and were bred an average of 3 services per conception with an average loss of 89 days from first service to pregnancy. Vibriosis in a range beef herd may be suspected when many cows continue to come into estrum in the latter part of the breeding season. The calving season is prolonged with a significant number of calves produced early followed by a period when relatively few calves are dropped and then late in the calving season more calves are born.^{28,36,79}

Pregnancy rates as low as 20 to 70 percent may be seen in some beef herds at the end of the breeding season. In other chronically-infected herds the pregnancy rates may be 60 to 85 percent with a poor conception rate in the virgin heifers. If routine vaccination of all breeding stock is practiced the pregnancy rate is usually from 80 to 95 percent.^{28,36,79} In an extensive field experiment it was reported that cows inseminated with semen from *C. fetus*-infected bulls had a much greater embryonic mortality rate and much lower nonreturn rate than with noninfected semen or with semen containing streptomycin.^{28,36,78} Cows bred with semen from infected bulls to which no antibiotic was added had a 42.7 percent conception rate compared to a 62.3 percent conception rate from similarly diluted semen from apparently noninfected bulls.

(4) Long estrous cycles ranging from 27 to 53 days with an average of 32 days are experienced by many recently infected cows and heifers.⁴⁶ Prolonged irregular estrous cycles of 25 to 60 days and even to 100 days are common following the first service of a susceptible female to an infected bull.^{6,21,41,75} This delayed or long interval may occur following any service in infected cows. Long cycles may be explained on the basis that fertilization takes place, the fertilized embryo may survive for 12 to 14 days or longer and is then killed or destroyed

by the *C. fetus* organisms, early embryonic death. If the fertilized ovum is destroyed prior to 14 days after fertilization then estrus will probably occur at the regular cycle length. Fertilization is apparently not affected by *C. fetus* infection.²⁰⁻²²

(5) Abortion was formerly considered the principal symptom of the disease. A 4 to 20 percent abortion rate of recognizable fetuses with an average of 12 percent in a herd was reported.⁵⁹ After reviewing the literature it was found that 3.4 to 29 percent of aborted fetuses from brucella-free cows were found positive on culture for *C. fetus*.⁶² An incidence of 8.6 percent of 1302 aborted fetuses were reported as positive for the presence of *C. fetus* in England.⁴¹ In both of these series a fairly large group of fetuses were so contaminated that recovery of pathogenic bacteria such as *C. fetus* was impossible. Of the 112 fetuses found positive in the latter study, 1 aborted embryo was recovered at 38 days, 1 at two months, 1 at two and one-half months, 5 at three months, 8 at four months, 30 at five months, 39 at six months, 15 at seven months, 3 at eight months, and 9 unknown. In a report on 198 aborted fetuses, the number of fetuses and the time of abortion was: 9 from one to two months of gestation, 14 from two to three months, 17 from three to four months, 29 from four to five months, 52 from five to six months, 36 from six to seven months, 26 from seven to eight months, 12 from eight to nine months, and 3 expelled dead at term. This was based on bacteriologic evidence in about 50 percent of the cases and on uncertain serologic evidence in the rest. Thus the greatest incidence of observed abortion is from 4 to 7 months of gestation. It is highly probable, according to our present knowledge, that abortions prior to 4 months are more common but are not observed and are considered as infertility or failure to conceive. Usually there is some indication of impending abortion after the fourth or fifth month of gestation by the presence of a vulvar discharge and slight edema of the vulva. Some enlargement of the udder may occur. In early abortions the placenta is usually expelled with the fetus. In late abortions retention of the fetal membranes may occur. Pyometra is rarely observed in *C. fetus* infection in cattle. The lesions in abortions at middle or late gestation are mainly in the fetal membranes, the fetus suffering secondarily because of interference with its circulation. The lesions resemble those of *Brucella* abortion. The intercotyledonary spaces are filled with a thick, purulent, viscid material. The cotyledons may be greyish white in color with much cheesy exudate between the maternal caruncle and the fetal cotyledon. The membranes may be thickened and edematous and the amniotic fluid turbid due to fetal diarrhea. *C. fetus* organisms may be found

in the placenta. The aborted fetus usually shows autolytic changes of subcutaneous edema; thin, bloody fluid in the body cavities; and a thick, yellow, flocculent, turbid material in the stomach that usually contains many *C. fetus* organisms. The stomach content of normal fetuses is clear, semi-liquid, and mucoid in nature.

Lack of libido in bulls—Infected bulls pasture-bred on susceptible cows copulate frequently. Because of the excessive sexual load occasioned by many of the cows returning to estrus, the bull may lose weight and libido.

Diagnosis—On the basis of the herd history or symptoms, a careful review of the breeding records, and a careful physical examination of the individual animals in the herd, including the bull, to be certain that no seminal pathology is present, a tentative diagnosis of vibriosis or trichomoniasis might be made. Since in most areas vibriosis is more common than is trichomoniasis as a cause for herd infertility and failure of conception, vibriosis is usually the diagnosis; but trichomoniasis should be suspected until sufficient tests have been made to make certain of the diagnosis.

Pyometra is rare in vibriosis but is occasionally observed in trichomoniasis. Abortions in trichomoniasis usually occur within the first four months and seldom after the fifth month of gestation while in vibriosis abortions in the fifth through eighth months are common. It is possible to find both vibriosis and trichomoniasis in a bull, a cow, or a herd. Herds with infertility due to sterile or infertile bulls with defective semen or infertility due to a lack of energy intake, especially in beef herds, may simulate the signs of vibriosis and a careful differential diagnosis is imperative.

Since vibriosis, similar to trichomoniasis, is not a systemic disease, antibodies are rarely found in the blood serum. Thus blood or serologic tests for diagnosing vibriosis are seldom used as reliable results cannot be obtained.

Since the infection in the female genital tract produces a local immunity, the agglutination test on vaginal mucus is useful for diagnosing the presence of vibriosis in a herd. Tests on vaginal mucus for the presence of antibodies to *C. fetus* was first described in 1949.^{71,75} This test was improved and made highly reliable for diagnostic purposes.^{6,39,46} The vaginal mucus from a cow or heifer infected with *C. fetus* gives a positive agglutination reaction approximately 30 to 80 days following the infecting service. This reaction persists in most cows for about 7 months or a range of 4 to 23 months. The mucus should not be taken from cows that have recently calved or for 3 to 4 days after estrus, as these cows may have metestrial blood in the mucus. Samples taken at these times may give false positive reactions. The excessive

amounts of mucus from cows in estrus should not be used for this agglutination test as false negative results may be obtained because the antibody level is diluted. In infected heifers only 21 percent of the vaginal mucus samples taken during estrus gave an agglutination reaction while 91 percent of samples taken agglutinated from about 4 to 5 days after estrus to 1 to 2 days before estrus.⁴¹ The agglutination test at the proper time on samples obtained from about 10 heifers which had been bred for the first time at least 2 months, but not over 9 months previously, should establish or disprove a diagnosis of vibriosis in a herd. The vaginal mucus agglutination test is most useful in dairy herds where the stage of the estrous cycle of open cows is usually known and confinement of cows in stanchions is often possible.

The tampon method of collecting vaginal mucus samples was perfected.⁷³ The technique of collecting vaginal mucus samples consists of holding the cow's tail to one side and washing the vulva and adjacent parts with soap and water. The vulvar lips are held open, and the vulva rinsed with clean water; a plastic 12 inch speculum containing both a tampon made of a gauze pad with a 16 inch string attached and the placement rod is inserted into the vagina. The speculum should be pushed as far forward as possible, and then the rod pushed forward, moving the tampon out of the speculum and into the cranial part of the vagina. To prevent air from entering the vagina and ballooning it, the thumb should be held over the end of the speculum while it is being withdrawn. The free end of the string is tucked between the vulvar lips to prevent its being soiled by feces. The tampon is left in the vagina at least 20 minutes to absorb an adequate sample of mucus. To remove the tampon wash the cow's vulva again, grasp the string and pull out the tampon and place it and the string in a plastic sample bottle. Samples should be kept in a refrigerator until mailed or taken to the laboratory. Inasmuch as no preservatives are added to the samples, they should not be sent through the mail over weekends or holidays to avoid spoilage. The necessary equipment may be supplied by the laboratory or made by the veterinarian. The use of a human vaginal tampon introduced into the cow's vagina with a plastic insemination pipette and transported in 4 ounce plastic bottles available in supermarkets has been described.³⁹ The laboratory should be sent an unused tampon and bottle for weighing. This is necessary to ascertain the amount of mucus present in each sample for dilution purposes. Care should be taken that infection is not spread from cow to cow. Separate equipment is necessary for each animal. Only certain vibrio antigens were suitable for the vaginal mucus agglutination test. Those that give too many false positive reactions when tested on virgin heifers

should be discarded.⁶ Any titer is significant but 1:25 is considered suspicious and 1:50 or more is positive.^{38,39} The number of positives in a representative sampling would vary, but one positive animal is probably sufficient to establish the presence of the infection in a herd.

Cultures of vaginal, cervical or uterine mucus taken at estrus from heifers and cows by pipette have been described.⁷⁵ Culturing of cervical mucus was the preferred method of diagnosing vibriosis in range beef herds as the animals only needed to be handled once and samples could be taken at any stage of the estrous cycle or even during pregnancy.^{28,23} Artificial insemination pipettes attached to 2-1/2 ml plastic syringes to produce a vacuum were adapted to collect cervical mucus samples.^{10b,28,30,33} The pipettes were passed through a sterile plastic or glass speculum to avoid contamination in the vestibular area. The pipettes were sealed with polybulbs and shipped to the laboratory in dry ice; freezing the pipettes in liquid nitrogen was not satisfactory because of breakage. The efficiency of recovering *C. fetus* from frozen vaginal or cervical mucus samples in the laboratory drops about 20 percent after 2 days in dry ice.¹⁰ This technique must be performed carefully and samples taken promptly to a laboratory for culture. In 88 samples of mucus from artificially- or naturally-infected heifers, vibrios were recovered in about 26 percent of the samples.⁴⁷ In another study 83.1 percent of the samples of mucus recovered from infected heifers at the time of estrus were positive on culture while only 26.5 percent of samples collected at other phases of the cycle were positive.⁴¹ Positive cultures were obtained from vaginal mucus samples taken by a specially-designed instrument, from animals recently bred, repeatedly bred, after calving, and after conception. A total of 429 vaginal mucus samples were collected and 26 percent were positive for *C. fetus*.²¹ Positive isolations from vaginal mucus were made as early as 11 days and as late as 224 days after conception. Positive cultures were obtained from 8 cows 21 to 196 days after calving. In a total of 114 vaginal mucus samples from 71 known virgin heifers none was positive for *C. fetus*. On routine examination of *C. fetus*-infected cows or heifers *C. fetus* was recovered from vaginal mucus in 76 percent of the cattle for only 40 days; in 12 percent the organism was found for 2 to 6 months; and in the remaining 12 percent for 7 to 12 months.²¹ About 50 percent of heifers were positive on culture one week after exposure to *C. fetus*.³³ From 3 to 9 weeks after breeding large numbers of vibrio were present in the samples. During the first 3 months after exposure nearly all open heifers, 80 to 90 percent, were positive so at this time random samples from 6 to 10 open heifers in a herd would be adequate for a diagnosis.

In cattle exposed 6 months previously only 20 percent were positive so 20 samples of mucus should be taken from open heifers or cows at this stage of the infection. Samples taken at the time of calving gave poor results. A biopsy instrument to recover the organism from the uterus of infected cows or heifers was described.⁷⁵

Culture of *C. fetus* from semen and preputial smegma—Although the other diagnostic tests are very useful, the isolation of *C. fetus* is the only unequivocal test. When cervicovaginal mucus can't be cultured promptly after collection the F.A. test is the best.³ Cultures of *C. fetus* can usually be recovered by a well-equipped laboratory with trained personnel. In culturing 306 ejaculates taken in as sanitary a manner as possible from 81 infected bulls vibrio were recovered in 20 percent of the samples.³⁸ In 307 samples on another trial *C. fetus* was recovered 20 percent of the time, or once in 5 ejaculates.²¹ The culturing of preputial smegma samples taken in the same manner as for recovering trichomonads was described.^{67,82} This procedure was more accurate than the culturing of semen samples. Special techniques were necessary because of bacterial contaminants in the prepuce. A fluorescent antibody screening test was developed to use on preputial and vaginal mucus samples; a positive test required confirmatory vibrio cultures, since certain *C. fetus intestinalis* strains and occasional *C. fecalis* strains fluoresced.^{80,82}

Another rather cumbersome technique used to detect *C. fetus* in bulls is to breed them to 2 or more virgin heifers and obtain vaginal mucus for culture from the fifteenth to the thirtieth day.²¹ After inseminating 1 ml. of undiluted semen into the cervical canal of 2 or more virgin heifers during estrum, samples were taken from the uterus 4 days after service and once a week thereafter, regardless of the phase of the cycle. In 8 heifers bred in this manner to known infected bulls 32 of 35 uterine biopsy samples were positive for *C. fetus*, while only 15 of 35 vaginal mucus samples taken at various times in the estrous cycle were positive on culture.^{1,2} This technique resulted in a positive diagnosis 14 days after breeding the heifer. Later, as a means of diagnosing vibriosis in a bull it was recommended to take 3 ejaculates from a bull in the same vagina, and douche the prepuce with saline solution. The semen and saline douche fluid were mixed and centrifuged. One ml. of sediment was inseminated into the cervix of a heifer in estrum and the heifer was cultured as described previously.^{60,61}

Procedures have been developed so veterinary practitioners can collect vaginal mucus, semen or preputial samples in the field in a proper manner and have them reach the laboratory in satisfactory condition for culture. More laboratories are being equipped with facilities and

personnel for performing this culturing technique. The fluorescent antibody technique aids greatly in the diagnosis of vibriosis by detecting *C. fetus* in cervical mucus cultures.⁴³

Aborted fetuses should always be cultured as this is one of the easier methods of diagnosing the presence of *C. fetus* in a herd. Immediately following abortion the fetus and possibly the fetal membranes if clean and not heavily contaminated should be taken to the laboratory for culture. The stomach contents and lungs are the organs in the large fetus from which *C. fetus* may most commonly be cultured. In small fetuses the amniotic fluid may be cultured. Some workers have reported finding the organism on direct smear or by fluorescent antibody techniques or culture of the stomach contents or exudate on the fresh cotyledons of the placenta.²⁴ If the fetus is small and cannot be taken immediately to the laboratory in the fresh state, it may be frozen, packed in dry ice, and sent by special delivery. If the fetus is large, the esophagus, duodenum and trachea may be carefully ligated and the stomach and lungs removed and handled as above. Ten to 39 ml. of stomach fluid from the aborted fetus may be removed in an aseptic manner and placed in a sterile vial. This may be frozen and shipped. If the fetus lives for even a short time, usually the stomach contents are contaminated by many bacteria. It is often possible in abortions caused by *C. fetus* to obtain pure cultures of this organism from the stomach contents of the fetus. The finding of the organism is a certain diagnosis that *C. fetus* is present in the herd. A differential diagnosis should be made between *C. fetus venerealis* and *C. fetus intestinalis* in cases of bovine abortion.

Prognosis—In vibriosis the prognosis in the cow is usually favorable as the infertility ordinarily is temporary in nature and after a period of 3 to 6 months most infected cows develop immunity to the infection and conceive. The greatest loss is economic and is due to the delay in conception. Most cows if they abort conceive after a suitable period of sexual rest unless a secondary infection produces permanent damage. Old bulls remain chronically or permanently infected unless isolated and treated. In many young bulls the infection is transient and disappears when they are removed from service.

Treatment—Our present knowledge is adequate to largely control vibriosis in beef herds and to eradicate the disease in dairy herds. Basically, the control methods are the same as in trichomoniasis. Genital contact between infected and noninfected animals should be prevented. Presently systemic vaccination with bacterins is highly effective in controlling infertility due to vibriosis in cattle.^{5,10a,b,28,40}

In a dairy herd the best and easiest way to control

vibriosis is to breed only artificially with semen from noninfected bulls; or with semen from infected bulls, that has been diluted or extended at least 1 to 25 with extender to which 500 to 1000 units of penicillin and 50 to 1000 micrograms of streptomycin or other effective antibiotics for each ml. of extender have been added. This extended semen should be held at refrigerator temperature for at least 6 hours before use. The semen should be collected, diluted, cooled, and held according to methods outlined in the chapter on artificial insemination, to assure maximum sperm survival. The handling of infected semen in this manner will, by the time of insemination, destroy any vibrio organisms present.⁵⁴ Vibrio-infected semen diluted 1 to 4 with extender without antibiotics resulted in 26, or 86.6 percent of 30 heifers becoming infected with vibriosis after insemination.^{38,45} When the infected semen was similarly diluted 1 to 25 with an extender without antibiotics and used to inseminate 29 heifers only 4, or 13.8 percent, became infected. This indicated the value of dilution in reducing the incidence of infection. In 94 heifers inseminated with infected semen diluted 1 to 25 with extender to which 500 units of penicillin, 500 micrograms of streptomycin and 3 mg of sulfanilamide per ml. had been added, then stored for 6 hours, none developed vibriosis. *C. fetus* was not isolated from 99 "repeat breeding" cows and heifers and cows from 7 herds that had been artificially inseminated with antibiotic treated semen from known infected bulls.^{21,22} Streptomycin alone was as effective as combinations of streptomycin and penicillin and sulfanilamide in controlling the spread of *C. fetus* in the semen.⁷⁸ The author has never recovered a fetus positive for *C. fetus* from an aborting cow that had been bred only artificially with antibiotic-treated semen. However the use of antibiotics in semen was considered an uncertain method of controlling vibriosis. The author knows that on the basis of the above data and his experience this method is highly effective but agrees that it is a thin line of defense against the disease. Bulls used for artificial insemination should be free of vibriosis to be certain that they cannot accidentally spread *C. fetus* in the semen.

The control of *C. fetus* in frozen semen is more difficult than in the extended liquid semen because the glycerol interferes with the effect of the antibiotics on the organism. Evidence was presented to show that frozen semen from vibrio-infected bulls extended with egg-yolk-citrate buffer with penicillin and streptomycin added in the proportions of 500 to 1000 units and 500 to 1000 ug respectively, did not produce vibriosis or infertility when used for the insemination of virgin heifers.⁴⁴ Although ampules of recently frozen semen may contain

viable vibrios holding frozen semen for several weeks resulted in their destruction. This has been confirmed over the past 20 years as very few cases of vibriosis have been reported in cattle bred with properly treated frozen semen. Two heifers were reported to have been infected with frozen semen stored for a year in an antibiotic and glycerol extender.⁵¹ Such occurrences are probably rare. The addition of 500 units of polymyxin B sulphate, 500 units of penicillin and 1000 ug of dihydrostreptomycin per ml. of extended frozen semen also was an effective means for the control of vibriosis.⁷² Recent studies have shown the importance of the antibiotic treatment of raw semen before it is extended and frozen and to evaluate the efficacy of antibiotic treatment procedures with each extender and processing technique used by the AI industry to prevent the spread of *C. fetus* in semen. Antibiotic treatment of *C. fetus*-infected semen extended in 3 common extenders did not eliminate the organism in one of them.^{36b}

In controlling vibriosis in a herd, artificial breeding to a noninfected bull, or to an infected or suspect bull after proper dilution and treatment of the semen with antibiotic and storage before use, should probably be continued for at least 2 to 3 years, in light of work indicating that vibrio will survive in the cow for only a short time in 75 percent of the animals, for longer periods of 2 to 12 months or more in another 24 percent of the infected females, and in a few cows for as long as 196 days after the termination of a normal pregnancy initiated by infected semen. Further work is necessary on this aspect of the disease. A total insemination program for most beef herds is impossible to accomplish so other control methods, particularly vaccination are necessary.

Some veterinarians advocate a period of 3 month's sexual rest for the acutely infected herd, after which breeding can be resumed with the infected bull or by artificial insemination inasmuch as within this time the cows have probably developed a satisfactory degree of immunity or resistance to the infection. The value of a 3-month rest period is questionable except to conserve the bull, as some females recover more promptly than others and if these were withheld from service the economic loss would be unnecessarily increased. Following natural infection a good immunity to vibriosis is produced that lasts from one to three years.^{2,8,31} The virgin heifers may be bred to young virgin bulls, which should continue to be used on them for the second pregnancy and thereafter. The infected bulls may be mated to the infected, immune cows and this program continued until the infected herd is eliminated. This procedure is difficult to follow over a period of years without an accident that would allow the infection to spread by venereal con-

tact from the infected cows or bulls to the vibrio-free herd.

In beef herds where artificial insemination is impractical and the maintenance of two herds, a clean one and an infected one, is not possible, vaccination each year with a commercially-available adjuvant bacterin of all animals of breeding age a few months before the breeding season is indicated. Vaccination with a proven highly antigenic bacterin at either one or two intervals provides a good level of immunity even in virgin heifers bred to infected bulls.^{5,11,12,23,35-36,40,43,52,57} Although *C. fetus* organisms may occasionally be found in the genital tract of vaccinated heifers soon after service to infected bulls, conception occurs promptly and the organisms disappear rapidly in most animals due to the presence of antibodies of the IgG variety.¹³ But a vaccinated animal may be a short-time carrier of the infection and infect a susceptible bull that serves her. This resistance produced by vaccination is usually sufficient to overcome the carrier state in cows¹³ and possibly bulls.^{5,11,40} Conception rates of 90 percent are common in vibrio-positive beef herds following vaccination. Commercial adjuvanted vaccines (Vibrin, Norden Lab, Bo-Vibrio, Armour-Baldwin Lab. and Tri-vib, Fort Dodge Lab.) with either one to three strains of *V. fetus venerealis* and others, some combined with leptospiral vaccines appear equally effective in cattle herds in producing immunity and controlling the disease in the U.S. when given once a year. Vaccination of heifers 6 months or more before the breeding season may result in some loss of immunity by the time of service to an infected bull. Even though a good degree of immunity is present a year or more after vaccination, yearly vaccination 10 to 14 days before the breeding season is recommended.⁴ It is advised in order to maintain a high level of immunity and better conception rates. Vaccinal immunity and convalescent immunity decreased from 1 to 4 years after vaccination or exposure.^{10a,b,31} So an annual single vaccination of all cows in infected herds 30 to 120 days before breeding is usually recommended.

Systemic vaccination with an adjuvant bacterin produces sufficient IgG to protect the cow or heifer against uterine infection even though antibodies in the blood are low.^{13,24} Thus by means of either artificial insemination with properly controlled vibrio-free semen, separation of the herd into vibrio-free and vibrio-infected groups with proper isolation and control, by yearly vaccination with a bacterin of all breeding females or by a combination of these methods vibriosis as a cause of infertility in a herd can be controlled.

Treatment of individual cows by the intrauterine infusion of about one gram of streptomycin together with

penicillin in an aqueous or oily base has proven quite effective in controlled studies in eliminating the vibrio organism from the female genital tract. Elimination is most efficient if given within 24 hours after service to an infected bull.^{1,15,49,74} Practitioners evaluating such treatments should realize that within a few weeks after the initial infection and endometritis most cows are developing immunity and recovering from the disease. Treatment of infected cows, unless it closely follows the infective service, is in reality being given to convalescent animals. Thus antibiotic infusions of infected cows are of limited or uncertain value.

The treatment of bulls for vibriosis—Most young infected bulls have only a transient short-term infection and then spontaneously recover in a few weeks or months if the organism is not reintroduced into the prepuce. Twenty-two young bulls were repeatedly exposed preputially to *C. fetus*. They became long-term carriers between 40 and 70 months, 3 and 5-1/2 years, of age. Four of these bulls developed a temporary carrier state of 4 to 29 days prior to the long-term carrier state. The use of young bulls to limit spread of *C. fetus* is of dubious value. Vaccination of bulls is a better preventive measure.^{10b,15b} Bulls over 5 years of age may remain permanently infected although occasionally even old bulls will spontaneously recover from the disease.¹⁰ Bulls do not develop a long-lasting or permanent immunity to the infection. However effective vaccines incorporating large amounts of antigens and adjuvants have been developed in Belgium and Australia that will apparently produce sufficient immunity to terminate natural and prevent new infection in bulls.^{5,11,12} With immunized bulls temporary or passive contamination of the penis and sheath after breeding an infected heifer is not an important or significant factor in the spread of genital infection of *C. fetus*.^{12a} Only 1 of 47 susceptible heifers bred by a vaccinated bull shortly after service with an infected heifer developed an infection with *C. fetus*.

Although bulls are usually vaccinated with bacterins in the U.S., it should be noted the *C. fetus* lives commensally in the crypts and on the surface of the epithelium of the prepuce without producing any inflammation. Therefore it is difficult to envision circulating IgG diffusing into the prepuce and eliminating the organism unless there is enough "inflammation or trauma" produced at repeated copulations. Large repeated doses of vaccine might prevent or cure infection in bulls.^{10b,40} Further studies in the U.S. with available vaccines are needed.⁴⁰ If bulls are cured with antibiotics or vaccines they may readily be reinfected. There is little value to eliminating infection in a bull if he is to remain in natural service in infected herds. In an AI stud it is highly de-

sirable to eliminate vibriosis from all bulls even though the addition of antibiotics to the semen has proven quite effective in controlling vibriosis. Swedish and Danish AI studs have eliminated vibriosis and this was accomplished in a large AI stud in the U.S.A.⁴² Prior to treatment of bulls rigid control measures on the movement of bulls and hygienic measures in the collection of semen were instituted. All bulls in the stud were tested semi-annually by culturing and immunofluorescence of preputial smegma samples. Each new bull entering the stud was tested similarly during the isolation period of several months. All bulls infected with *C. fetus venerealis* were treated with 5 gm. of dihydrostreptomycin sulfate in 10 ml. of a 50% aqueous solution infused in the preputial cavity and massaged thoroughly through the skin of the sheath for 5 minutes while the preputial orifice was closed. This was repeated daily for 5 treatments. At the time of the first and third treatments two subcutaneous injections of 22 mg/kg of body weight of dihydrostreptomycin were given.⁴² Repeated tests of preputial mucus were conducted at biweekly intervals after treatment. Test breeding of virgin heifers to treated bulls followed by repeated cultures of the cervical mucus of the heifers could be done to determine if the treated bulls had eliminated the infection. This technique is more costly than the direct sampling of the preputial smegma. Treatment produced mild focal reddening and ulcerations of the penile mucosa that healed promptly. Other antibiotics in the treatment of vibriosis in the bull have been tried because of fear of producing streptomycin-resistant vibrio organisms, since streptomycin is also used to control the organism in semen. These antibiotics, tylosin and furacin have not proven as effective as streptomycin in the treatment of infected bulls.

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BRUCELLOSIS

Brucella abortus infection has been discussed previously under the section on abortion, (See Chapter V) as that is the principal characteristic of the disease. However, evidence indicates that *Brucella* infection of the uterus plays a definite role in infertility even though infertility and endometritis did not occur in the recently infected nonpregnant animal.¹⁷ The role of the bull in the transmission of brucellosis is minor but interesting. According to early field observations, the bull was gen-

erally supposed, to be one of the more important factors in the spread of the disease. But the transmission of brucellosis from infected bulls to susceptible cows by natural service has not been demonstrated in controlled experiments. Infected bulls when bred naturally to heifers in estrum rarely spread the disease even when the prepuce had been artificially contaminated with *Brucella* organisms prior to service.^{54,55,75} However, it has been demonstrated that susceptible cows artificially inseminated into the uterus with infected semen from a positive *Brucella*-infected bull would develop brucellosis.^{16,54,55} Most infected bulls harboring foci of infection in the genital tract discharge *Brucella* organisms intermittently in the semen, but one bull had viable organisms in 80 consecutive ejaculations over a period of 18 months.⁵⁵ The uterine infection produced in heifers by intrauterine insemination of infected semen resulted in impaired fertility; only 1 susceptible heifer conceived on the first service out of 12 inseminated; 8 of the 12 susceptible animals became infected; only 2 infected animals conceived, and 1 of these aborted at 104 days of gestation. Each animal was inseminated an average of 3.5 times. The infertility was temporary, lasting 3 to 12 months. These results were interesting when compared with 12 other susceptible heifers bred artificially to the same bull but with the semen being inseminated into the external os of the cervix; 9 of 12 animals conceived on the first service.^{31a} From these experiments *Brucella abortus* should be included with *C. fetus* and *T. fetus* as an agent that can and will produce infertility or temporary sterility when introduced into the bovine uterus. Under natural conditions *B. abortus*, not being motile, cannot invade the uterus from its vaginal deposition as can *C. fetus* and *T. fetus*. This is a further reason for inseminating cows by placing semen into the cervical canal rather than into the uterus.

Intrauterine insemination may introduce other pathogenic bacteria that may cause failure of conception, endometritis, and temporary sterility especially if insemination is done late in the estrous period or in metestrus when the genital tract is under the influence of progesterone. Following abortion due to *Br. abortus*, a sexual rest period of 90 days or more and possibly several uterine treatments may be necessary to aid involution and recovery of the endometrium necessary for conception. Aborting animals should be isolated, as ingestion of infective material and discharges from the genital tract is the most common means of spreading brucellosis.

Further evidence of the adverse effect of *brucella* infection of the uterus was a report²⁰ that sterility was 4 times more frequent in suspects and 8 times more frequent in *Brucella* reactors than in negative animals. *Brucella*-positive cows averaged 2.8 services per conception

following normal calvings and 3.6 services per conception following abortions.⁶¹ Other evidence of this type was cited.⁶⁵ A more severe endometritis was present in infertile *Brucella* positive cows than in infertile *Brucella*-negative cows.¹⁸ These many reports serve to emphasize strongly the role of ***Brucella abortus*** in causing infertility in a herd, and the necessity of controlling this disease to prevent severe economic losses due to reproductive failure and abortion.

GRANULAR (NODULAR) VENEREAL DISEASE (GRANULAR VULVITIS) AND MYCOPLASMA, UREAPLASMA AND HEMOPHILUS INFECTIONS

According to Williams this disease was first described in Switzerland by Isepponi in 1887 as a cause for infertility and abortion.⁸² Since that time there has been much debate on whether or not the disease is an important cause of infertility. Most workers agree at present that there is no evidence linking this disease with abortion. Williams stated: "It may be said to be a lesion without a known cause and regarding the effect of which there is scant knowledge." No disease of the reproductive system of cattle has been so unproductive of conclusive results on research as has granular venereal disease. Only in the area of histopathology is there any agreement on the nature of this disease. The lesions and the mucopurulent vulvar discharge often following service, are readily noted by both farmers and veterinarians. Therefore granular venereal disease or granular vulvitis has frequently been incriminated as a cause for infertility in cattle. The term granular vaginitis used to designate this disease is a misnomer as the papules or granules are largely limited to the vulvar mucosa and are only sporadically found in the vagina.⁴⁵

The disease is seen most commonly in heifers during the breeding period for their first and second pregnancies. The condition has been noted occasionally in calves as young as 11 days of age and in heifers prior to puberty. It is less acute and severe in middle-aged and older cows. It is observed most commonly in postpartum heifers and cows especially following natural service and less commonly as pregnancy progresses toward term. It is rarely observed at the time of parturition. Granular venereal disease is seen in practically any herd at any time of year with an incidence varying from 10 to 90 percent of the cows or heifers. Occasional acute herd outbreaks are observed that spread rapidly through the herd and even affect prepubertal heifers. This may be due to the vulvar sniffing which is common in cattle. This may carry the organism from the nose of one animal to the vulva

of the other.^{13,23-26,51} Since the mycoplasma and *Hemophilus* organisms are commonly found in the respiratory as well as the lower genital tract spread of infection is favored by this behavior. The lesions differ greatly in severity between heifers and cows in a herd. In general the disease occurs more commonly and more severely in young cows or heifers being bred naturally by the bull than in those being artificially inseminated. The lesions of this condition may be observed on the penis and prepuce. The lesions are present more commonly in bulls serving cows naturally than in bulls in an artificial insemination stud that ejaculate into an artificial vagina. The disease in bulls should be called **granular venereal disease** or **granular balanoposthitis**.

The mode of spread of the disease is not known, but apparently if it is due to an infectious agent, it is spread rapidly and easily. This is difficult to prove, inasmuch as isolated control heifers may develop the condition. This condition in cows more properly should be called a granular vulvitis. In the acute stage in cows these nodules are reddened and highly inflamed, causing a mucopurulent type of discharge that may mat and hang from the vulvar tuft of hairs. If these cattle are bred by a bull, or if a speculum is passed, the granules or nodules are likely to bleed. The cow or heifer in this acute stage exhibits some pain when the vulvar lips are handled and may exhibit irritation and pain when urinating, as well as by not standing quietly to be bred. In these acute severe cases there are many nodules, usually appearing confluent and tending to be in ridges or rows on the top of the folds of mucous membrane. The vulva may be slightly swollen. Occasionally discrete, 2 to 5 mm, white inclusion cysts containing an exudate may be observed in the dorsal commissure or lateral walls of the vulva.^{23,25,45} Bulls with acute severe lesions may occasionally refuse to copulate or will be slow to breed. Coitus tends to aggravate the lesions especially in heifers with a small vulva that are bred to a large bull. In mild and chronic cases of granular venereal disease the lesions are few in number and are usually found around the lower half of the vulva and around the clitoris. The chronic nodules are pale yellow in color and no exudate or inflammation of the mucosa is apparent. Following breeding the granules that were pale before breeding ordinarily become congested and reddened. Thus chronic lesions may become acute. But chronic lesions are much more common especially in cows the last half of the gestation period.

These nodules or granules histologically are lymph follicles, lymphoid accumulations, or hyperplastic lymphoid elements beneath the mucosa and therefore the disease may be a normal response to various insults. It is interesting to note that similar lesions have been de-

scribed in the dog.¹ In the male dog a follicular balanoposthitis with hypertrophied lymph follicles may occur. In the bitch similar lymph follicles in the vulva were described. These lesions are common in the genital tract of sheep, goats and swine, but in a mild form.^{1,45,82}

These granular or papular hypertrophied lymphoid lesions in the mucous membrane are similar to those observed beneath the third eyelid in follicular conjunctivitis in dogs and in follicular pharyngitis in horses. These latter two conditions are usually ascribed to and associated with bacterial or possibly viral infections.

The cause of granular venereal disease has been ascribed in many reports over many years as due to *Streptococcus vaginitidis*, a hemophilus-like pleomorphic rod, a virus and other organisms, mycoplasma, *C. pyogenes*, *Staphylococci*, and *E. coli*, and most recently ureaplasmas or T.-mycoplasmas and *Hemophilus somnus*.^{1,2,22,23a,b,26b,43,51,69}

Mycoplasmas or ureaplasmas are very small bacteria that lack a cell wall. They are commonly found in the upper respiratory tract and lungs and the vagina and vulva of cattle and also humans.^{1,13,21,23a,b,26b,31b,50,51,62,73} They are generally susceptible to the tetracycline antibiotics.²³ Mycoplasmas and ureaplasmas vary greatly from non-pathogenic to pathogenic strains. Some authors, indicate they may be part of the normal flora of the vagina and vulva and prepuce and penis. They are seldom found in the uterus and oviducts.^{13,21,62,73} Pathogenic ureaplasmas were inoculated into the uterus or cervix of 23 virgin heifers, 16 of 19 heifers developed granular venereal disease lesions in about 4 days from which the organism could be isolated for 13 to 41 days. Clinical cases of the disease persisted for several months. However the ureaplasma could only be isolated from the uterus or uterine tubes for 1 to 7 days. Only a short-lived endometritis and salpingitis were produced.^{25,26} When heifers were bred naturally to a bull infected with *Mycoplasma agalactiae* var *bovis* the IgA levels in the vagina rose to high levels while the IgG levels in the noninfected uteri remained low. Thus this reaction resembles that seen in vibriosis. The evidence indicates that IgA provides protection for the animal in the superficial areas such as the vagina and the nasal cavity and the IgG provides protection for the deeper organs of the body such as the uterus and lungs.²¹ One study showed that pathogenic ureaplasma (T. mycoplasma) could cause cessation of ciliary activity, ciliary collapse and sloughing and finally disorganization of epithelial tissues with necrosis and desquamation⁷³ which might explain the underlying cause of infertility when these organisms affect the ciliary activity of cells in the cervix, uterus and oviducts of upper genital tract of cows.

These studies, though quite convincing,^{23-26,71} require further confirmation as others have doubted whether a specific agent is the cause of bovine granular venereal disease.^{45,70}

The incubation period for the development of the acute stage of granular venereal disease is short, 2 to 5 days, after exposure or breeding with the formation of nodules or papules in the vulva and around the clitoris that are red and inflamed and result in a mucopurulent discharge. The acute phase gradually recedes over the next 2 to 3 months unless reinfection occurs. But this latter response is much less severe than the initial reaction.^{25,26} Others have reported a 2 to 3 week incubation period with an increase in severity and number of granules developing, through the eighth week.²² The lesions of granular venereal disease consist of small elevated papules or granules found mainly on the vulvar mucosa just inside the vulvar lips most commonly in the region around the clitoris. (See Figure 105.) In more severe cases the granules may extend up the lateral walls of the vulva to the dorsal commissure. Diagnosis is based on the clinical signs and lesions of granular venereal disease.

In the 1950's about 10 percent of 2530 cows were found affected with granular venereal disease.⁷⁶ The fertility of affected animals was 6 percent lower than that of the other 90 percent. Of 4616 cows being bred by artificial insemination; 49 percent had no evidence of granular venereal disease; 44 percent, or 2,065 had mild symptoms; and 7 percent, or 289 cows, had severe lesions.⁷⁶ The conception rates on first service in each group were 68.9 percent, 65.7 percent, and 58.1 percent, respectively. Therefore the difference in rates was significant. Whether *C. fetus* was present and influencing these results was not reported. A temporary infertility was as-

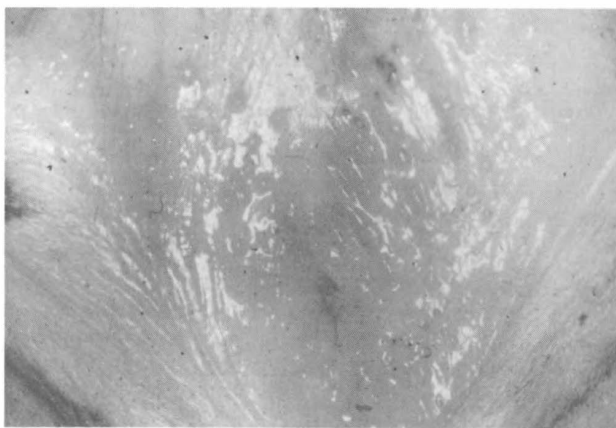


Figure 105. Granular Venereal Disease in a Heifer—Note the concentration of lymphoid follicles around the clitoris.

sociated with granular venereal disease.²²

Canadian researchers^{23,26,50,51,62} have isolated ureaplasma (T. strains of mycoplasma). **Mycoplasma bovinegenitalium** and **Hemophilus somnus** from clinical cases of granular venereal disease. Ureaplasmas were isolated from 100 percent of acute granular vulvitis cases, from 74 percent of chronic cases and from 23.5 percent of normal herd mates.²³ Recent advances in laboratory culture methods, special transport media,⁵¹ refrigeration and rapid transport to the laboratory are necessary to isolate these organisms.

These organisms are commonly found in the external genital organs, vulva and prepuce, and respiratory tract of cattle. Mycoplasma which encompass many species of achleoplasma, including **A. laidlawii**, and **M. bovinegenitalium** and **M. (agalactiae) bovis** and the ureaplasmas of which there are many species, are found on serosal or mucosal surfaces of the urogenital and respiratory tracts, mammary gland, joints and eyes. **Hemophilus somnus** is a Gram negative coccobacillus that causes septicemia, pneumonia, thromboembolic meningo-encephalitis, probably the calf diphtheria syndrome in feedlot or young cattle, and arthritis.⁵¹ These organisms may be found in both normal and diseased animals. Further studies are indicated to differentiate the pathogenic and non-pathogenic species of these organisms by serologic or other methods and to better understand their role in abortions, granular venereal disease (vulvitis and balanoposthitis), endometritis, toxic metritis, salpingitis and seminovesiculitis in cattle and other animals. It should be further noted that mycoplasmas and ureaplasmas also cause infertility, abortion and urethritis in humans.^{31b,40}

The prognosis is usually fair to good in granular venereal disease but in acute cases it may be 2 to 4 weeks or more before the acute signs subside. As far as completely curing the condition in cows and bulls the prognosis is guarded, as sometimes several months or more are required. Granular venereal disease may remain chronic, or acute lesions may recur. In longstanding cases in bulls, the lymphoid enlargements may become fibrotic. If a high incidence of early embryonic deaths occur with this disease one should suspect a combined infection with **C. fetus** and/or **T. fetus**.

Mycoplasma bovinegenitalium, ureaplasmas and **Hemophilus somnus** were isolated from acute cases of granular vulvitis or granular venereal disease in cattle associated with a purulent discharge, endometritis and infertility. This acute form of the disease was seen most commonly with intensive management, over-crowded, unsanitary free-stall barns, and heavily fed, stressed dairy cows and heifers in the winter.^{23-26,51} First service conception rates dropped from over 50 percent to 30 percent during the acute phase of the disease and returned to 50

percent after intensive therapy with postbreeding infusions of 1 gm of tetracycline or oxytetracycline into the uterus, cervix and vagina and using a sheathed or protected insemination pipette for AI or intrauterine infusions to reduce the numbers of pathogenic organisms carried from the vulva into the cervix and uterus. Since bulls carry these organisms in their prepuce and occasionally in their seminal vesicles, semen used for AI should contain levels of antibiotics to eliminate these organisms and prevent their spread. Minocycline HCL is effective in the control of mycoplasma and ureaplasma in the extended semen and lincomycin and spectinomycin controls mycoplasma. **H. somnus** is readily eliminated by a variety of antibiotics. Tetracyclines cannot be used in extended semen because of their harmful effect on spermatozoa. Granular vulvitis, endometritis and salpingitis have been produced experimentally by the introduction of certain of these three organisms, especially the ureaplasma, into the vulva, cervix and uterus. Based on early studies recovery from uterine infections and endometritis may be quite prompt.

The treatments for granular venereal disease are so many and varied that the author believes this condition fits into the category with other conditions treated with a similar wide variety of therapy in which probably any treatment within reason or no treatment at all would be equally successful. The older more commonly used treatments in affected cows and bulls are locally applied antibiotics and antiseptics but their value is questionable. When conception rates were greatly reduced, due to ureaplasma infections 1 gm of tetracycline in solution infused into the uterus cervix and vagina 24 hours after service gave encouraging results.^{23,26b} Treating the granular lesions in the vulva with irritating or cauterizing drugs appears to clinically result in the most rapid improvement in acute cases of granular vulvitis. They should not be used in bulls. These include 1 to 2 percent acriflavine ointment, straight Lugol's solution, or 4 to 5 percent silver nitrate solution repeated as needed every 7 to 10 days.

Since this condition tends to improve with time and since copulation aggravates the condition, breeding is stopped in the severe cases, especially in bulls, for several weeks or longer. The owners are advised to breed their affected cows and heifers by AI possibly using a small plastic speculum or tube to guide and protect the AI pipette so that it does not contact the vulvar mucosa.^{23,26b,51} This seems to cause no exacerbation of symptoms. If they cannot be bred artificially, a period of sexual rest for 2 to 4 weeks is advised in the severe cases. A killed vaccine is currently available for immunizing against **H. somnus** but its value in genital infections needs study.

In recent years investigations have resulted in ad-

vancing our knowledge of the mycoplasmas, ureaplasmas and Hemophilus organisms. The pleuropneumonia like organism (PPLO) now called **Mycoplasma bovis** is only mildly pathogenic in the female genital tract and is frequently isolated from the tract. **Mycoplasma bovis** was isolated from cattle in several herds suffering from infertility and occasional abortions.^{23a,28,51} In some cases ovarian adhesions and cervicitis were present; in others a mucopurulent discharge was noted several days after coitus. The organism was found in semen. Varying degrees of endometritis, salpingitis and adhesions between the fimbria and peritoneum was produced in 7 of 8 heifers receiving an intrauterine inoculation of a suspension of mycoplasma (**M. agal. bovis**) recovered from a case of bovine mastitis.³⁶ The doses used were considered to be excessive. This condition, produced experimentally, has not yet been described as a clinical entity. The **M. bovis** organism which is quite pathogenic for the female genital tract is seldom found there. The common occurrence of mycoplasma and ureaplasma in the prepuce of bulls and in the semen has been described under infertility in the male.^{1,2} It is questionable if many of the isolated mycoplasma spp. are pathogenic as heifers inseminated with infected semen samples did not become infertile. Only one group of isolates produced inflammatory changes in the endometrium. A study of many strains of mycoplasma by morphological, cultural and serologic means as an aid to separating pathogenic and saprophytic organisms has been conducted.^{1,2,5,6} Similar studies are needed with the ureaplasmas and **H. somnus**. Many mycoplasma cultures are a mixture of several strains, 166 pure strains were recovered by cloning, characterization and serologic techniques and 13 serotypes were found not including the bovine T. strains or ureaplasmas. Serotype B or **Mycoplasma bovis** caused vulvovaginitis, epididymitis, seminovesiculitis, arthritis and rarely mastitis.^{1,2,5,6,25,26} Serotype F or **Mycoplasma agalactiae var bovis** caused mastitis, endometritis, salpingitis, salpingo-peritonitis and abortion.⁴⁰ This type of organism was cultured from semen from a bull that when bred to heifers apparently produced conception but the animals came back into estrum in about 4 weeks and thereafter were infertile.⁶³

Acholeplasma (M.) laidlawii was recovered from the oviducts in 52 or 71 percent of 73 repeat breeders,⁴¹ while only 42 or 24 percent of 179 cows slaughtered for other reasons were infected. Lesions were found in 117 infected uterine tubes. Many workers^{1,5,23} consider this **Mycoplasma** nonpathogenic. It is possible that the early workers in studying this PPLO or mycoplasmal organism were actually dealing with vibriosis and recovered these rather ubiquitous mycoplasmas. This PPLO organ-

ism was found in semen in 94 percent of the bulls.³ Freezing of mycoplasma in semen had no adverse effect on the organisms,³⁹ and they were quite resistant to antibiotics commonly used in semen extenders.²³

Hemophilus spp. was reported to cause an outbreak of vaginitis and cervicitis in a herd of dairy cattle,¹² It was characterized by a copious, purulent, yellowish-white discharge from the vulva and a hyperemia of the vagina and cervix lasting for 2 to 3 months. The disease could be spread by coitus and resembled viral vaginitis described previously. The vulva was not affected. A hemophilus-like organism was described as a cause of granular vulvitis.²² **Hemophilus somnus** has been isolated from cases of granular venereal disease.^{25,26}

In a review of the role of the Mycoplasmas in diseases of bovine reproduction it was reported that mycoplasmas have been isolated from the genital tracts of cattle, humans, horses, dogs, pigs, goats and cattle.^{1,2} Those organisms associated with lower genital tract infections of granular vulvitis were **M. bovis**, **M. bovis**, ureaplasmas (**T. mycoplasmas**) and **A. laidlawii**. Those organisms associated with the upper genital tract infections of endometritis and salpingitis are **M. bovis**, **M. bovis**, **M. agalactiae bovis**, ureaplasmas and **H. somnus**. In bulls **M. bovis** and ureaplasmas and occasionally **M. agal. bovis** can cause seminovesiculitis and possibly orchitis and epididymitis and be present in semen.^{1,23-26,51}

Many more studies will be needed on mycoplasmas, ureaplasmas and Hemophilus organisms commonly found in the lower reproductive tract, vulva and prepuce and upper respiratory tract to determine the pathogenic and nonpathogenic serotypes and the mechanisms whereby they gain access to the upper reproductive tract, uterus, uterine tube, seminal vesicles and testes. These further studies are necessary to clarify the presently very confusing literature and clinical disease picture. With the rapid advances in microbiology and immunology in recent years the isolation of these organisms and the delineation of their importance, pathogenesis, epidemiology and therapeutic control measures should be forthcoming.

Other Bacterial Infections

Leptospirosis due to **L. pomona** has not been shown to be the cause of infertility or early death of fertilized embryos; although abortions, especially the latter half of the gestation period, are common. Statements that **L. hardjo** and **L. mini-szwajizak** have been associated with infertility in enzootically infected herds have appeared recently in the literature, a careful perusal of the articles

cited^{34b,36a} do not support this observation. Infertility associated with abortions, secondary retained placentas, and metritis and delayed conception are characteristic sequelae of any abortifacient disease including leptospirosis. Leptospiral organisms have not been shown to be a cause of early embryonic deaths or conception failure.

Streptococcal infection characterized by cervicitis was described in 1932 as a common cause for infertility in cows. This organism was frequently recovered from inflamed genital tracts of cows failing to conceive but it is unlikely that it was responsible for enzootic outbreaks of infertility. The author observed one herd of dairy cattle with much infertility characterized by a mucopurulent discharge from the vulva in some animals and early embryonic deaths with long intervals between services. On culture of the vagina of the cows at necropsy a pure infection of *Streptococcus dysgalactiae* was isolated. Endometritis was present. Sanitary conditions in the herd were marginal; all cows calved in the same calving stall. The bull may have spread the infection at the time of coitus.

Corynebacterium pyogenes has been described as a cause for failure of conception, for a persistent mucopurulent discharge from the vulva and even occasionally for permanent sterility.^{37,38} Apparently it gains entrance to the genital tract at the time of parturition or when a retained placenta is present. This organism causes a chronic postpuerperal metritis, endometritis, salpingitis, or pyometra with delayed involution of the uterus. This invasive organism may be difficult to cure and the prognosis should be guarded^{35b} (See Endometritis).

C. pyogenes infection of the postpartum genital tract is occurring with increasing frequency as the herds of cattle get larger and close confinement, "zero pasture," and overuse of a few calving stalls that are not properly "sterilized" between cows. In affected herds nearly 90 percent or more of cows calving in the infected environment or in those calving stalls become infected and develop a copious, yellow, mucopurulent discharge that lasts for 2 to 6 months resulting in great delays in conception even though eventually the infection is overcome and the cows conceive. Retained placenta and calf scours are also commonly observed in these same herds due to the unsanitary conditions. Since the infection obviously occurs at or soon after calving, having the cows calve in a different clean environment away from the contaminated facilities or at pasture often results in a prompt and dramatic reduction in clinical cases of vaginitis, cervicitis and metritis. Enough properly designed calving stalls that can be thoroughly disinfected or sterilized between calvings and/or moved, if portable, to a clean location are necessary for large free stall dairy herds.

A vulvovaginitis due to *C. pyogenes* occurring one to four days following coitus has been described.¹⁴ These infections persisted for 7 to 14 days but often recurred at a subsequent breeding to the same bull. Similar *C. pyogenes* organisms were cultured from the vagina of affected cows and the prepuce of the bull. An acute vulvovaginitis was reported due to *E. coli* toxins introduced by coitus with an infected bull.¹⁴ Signs developed within 4 to 6 hours of service and lasted for only several days.

Other low grade infections found in the genital tract of sterile or infertile cows or cows exhibiting a mucopurulent exudate include:

*Micrococci	
*Diphtheroids	
* <i>Pseudomonas aeruginosa</i>	
* <i>E. coli</i>	
Bacilli	
Staphylococci, albus and aureus	
*Enterococci and others	
Actinomyces	Yeast
Neisseria	Mycobacteria
Flavobacterium	Salmonella
Sarcina	Alkaligenes
Proteus	Gaffkya
Molds	Chromobacteria

*The organisms most commonly found.

These infections have been described as being found in the genital tract and uterus of cows that fail to conceive.^{4,27,35a,c,38,52} These ubiquitous organisms recovered from the bovine genital tract were mainly saprophytic strains in normal cows but in infertile cows the strains were primarily pathogenic.^{35a,c} Undoubtedly they may gain access to the tract at the time of parturition or breeding and if the conditions are favorable they establish themselves at least temporarily and possibly cause varying degrees of inflammation of the uterus, cervix, vagina, vulva, and oviduct possibly resulting in infertility. Twelve heifers artificially inseminated with semen from bulls with semino-vesiculitis due to *Ps. aeruginosa* developed varying degrees of metritis, cervicitis and vaginitis and the organism could be recovered in 4 of 8 heifers 44 days postservice.³² The discussion of the diagnosis and treatment of these nonspecific infections will be made later in this Chapter. (See Endometritis.) Cases of infertility due to these various wound-infection type of organisms are usually sporadic and not associated with an enzootic type of infertility. The organisms mentioned above, including streptococci, *C. pyogenes* and PPLO or mycoplasmas are ubiquitous and will occur in some cows despite proper management. Their treatment is largely

symptomatic. The same organisms are frequently present in bull semen but apparently seldom pass beyond the vagina and cervix to establish themselves in the uterus. *Pseudomonas*, coliforms, and staphylococci are more common in bulls' semen than in the genital tract of cows, probably due to contamination of the semen with organisms common in the sheath.

A condition similar to an enzootic venereal disease in naturally-bred cattle occurred in some artificially inseminated herds, with 15 percent or more of the cattle showing varying degrees of infertility even when neighboring herds of the same breed served by the same technician have less than 5 percent "repeat breeders."³¹ This condition may occur after 2 to 3 years of artificial insemination and no *C. fetus* or *T. fetus* are isolated from the cows. These workers were unable to isolate the causative organism or determine its mode of spread. Other researchers have found similar perplexing problems.¹⁷ In the future, therefore, possibly other organisms including viruses may be found as causes of "enzootic" infertility.

Necrotic vulvitis of feedlot heifers has been well-described. The cause is unknown. It has been observed in lots where hogs are present and injuries and vulvitis have been blamed on them. It may occur following rectal examination. Anovulvitis may be observed secondary to a diarrhea where an irritant is apparently present in the fecal material. Body temperatures may be slightly elevated for a few days but healing occurs in two weeks. Infertility in affected heifers has not been reported. It has been suggested that an allergic factor may be involved.

Actinomycosis—Two cases of actinomycosis of the bovine genital tract, characterized by large swellings that proved to be multiple sclerotic abscesses with extensive pelvic adhesions were described.⁸² One of these cases developed following a retained placenta. Actinomycosis is difficult to differentiate from tuberculosis but the swellings in the latter are more nodular. Due to the extensive lesions the prognosis was poor and both cases were cultured and diagnosed after slaughter.

Tuberculosis—Tuberculosis of the genital tract of the cow has not been observed the last 50 years in the Ambulatory Clinic of the New York State Veterinary College. With the almost complete eradication of this disease in the United States the opportunities for observing it in this country are very rare. However, in other countries where tuberculosis is still prevalent the infection may involve the female genital tract and produce sterility and abortion. Tubercular lesions of the vulva, vagina, cervix, uterus, oviducts, and ovary have been reported.^{11,82} (See Figure 106.) The disease usually affects the uterus and oviducts producing characteristic nodular swellings, enlargements and adhesions between the uterus,



Figure 106. Genital Bovine Tuberculosis—involving the ovaries and mesometrium.

(Courtesy of F. Megale.)

oviduct, ovary, surrounding broad ligaments, rectum, and other organs and tissues. The genital discharge from these lesions is usually non-fetid. In most cases the uterine involvement is bilateral, a fact which may differentiate the condition from other infectious or pathologic lesions of the uterus. Bovine tuberculosis due to *Mycobacterium bovis* is by far the most common type affecting the uterus and causing sterility and abortion. Occasionally the avian type may be found.^{29,68} This type is characterized by small abscesses about 0.25 inch in diameter, involving the endometrium. The avian type of tuberculosis is not readily diagnosed per rectum because of the lack of enlargement of the uterus or oviducts and the fact that adhesions do not develop. The tuberculin test may fail to detect animals severely affected with bovine tuberculosis. Avian tuberculin may be of assistance in diagnosing the avian form, although it is usually diagnosed on postmortem examination. Culture of the genital discharges together with the presence of characteristic nodular swellings and adhesions aids in the diagnosis of this disease. Severely affected animals are usually hopelessly sterile and should be slaughtered. In milder infections conception may occur, but abortion or retained placenta may result. Infection of the genital tract of the cow may result in the spread of tubercular infection to the penis and prepuce of the bull at coitus.

INFECTIOUS VIRAL DISEASES CAUSING BOVINE INFERTILITY

Infectious Pustular Vulvovaginitis (IBR-IPV)
(Vesicular Venereal Disease, Coital Vesicular
Exanthema, Infectious Balanoposthitis, Genital
Cowpox, or Blaschenausschlag)

This viral disease has been described previously with IBR-IPV abortion (See Chapter V) since the two diseases are caused by the same herpes viral agent. Infectious pustular vulvovaginitis (IPV) is described as a non-vesicular viral disease characterized by papules, pustules, but no vesicles, that rapidly coalesce to form a diphtheritic membrane that detaches leaving ulcers in the mucosa of the vulva, vestibule and vagina especially over the areas of the lymphoid follicles.^{33,46} Intracellular inclusion bodies can be found in affected cells in the mucosa of the genital tract. The cows exhibit an elevated temperature for several days early in the course of the disease. Edema, pain on urination, and a yellowish serous to purulent discharge from the vulva is characteristic of the disease. The ulcers, diphtheritic membranes and severity of the infection differentiates I.P.V. from granular venereal disease. The disease may spread rapidly through the herd and even affect unbred heifers. The respiratory and abortion forms of the disease rarely accompany the genital form. However rare outbreaks have been reported where simultaneous infections with the upper respiratory, genital and conjunctival forms of IBR-IPV, but no abortions, occurred.⁴⁹ Abortions in pregnant cows commonly occur after the respiratory disease but are only rarely observed following the genital form of the disease.

The cause for this is not completely understood. (See IBR-IPV Abortion, Chapter V.) Natural service by the bull may spread the disease as this virus may produce a balanoposthitis, but other means of spread such as by switching tails of cows confined in stanchions or grooming may also spread the disease from one cow's rear parts to the next. The farm dog licking the genital discharges on the vulvas of affected cows and then normal cows may transmit the disease. The IBR-IPV virus may be transmitted by artificial insemination in liquid or frozen semen and cause an endometritis and a temporary short-lived infertility.^{47,66,72}

Although this disease is rather common in Europe and Australia it is observed only occasionally in the United States. Even though IBR, the respiratory form of the disease, is common in New York State only 1 to 3 outbreaks of IPV are reported each year. A similar observation was made in California.⁷⁴ Two outbreaks occurred

in the same herd 4 years apart.⁶⁹ Similar reoccurrences of the disease in the same herds have been reported in Europe. In one study⁶⁶ when bulls harboring preputial infections of IBR-IPV were bred naturally to susceptible heifers lesions of infectious pustular vulvitis resulted but conception rates were normal. However if IBR virus was infused into the uterus after breeding infectious pustular vulvovaginitis developed and the conception rate was low, 40 percent. An increased number of services per conception was required due to the endometritis and salpingitis produced. About 30 percent of the estrous cycles were shortened due to the endometritis.⁶⁶

The onset of the disease is rapid and within 3 to 6 days involves 60 to 90 percent of a herd; the incubation period is short, usually 48 to 72 hours. Similar lesions occur on the penis and prepuce of affected bulls. Affected bulls may refuse coitus. Although infectious pustular vulvovaginitis interferes with breeding until the lesions heal, this form of the disease is not known to result in sterility, infertility, or abortion.

The prognosis is generally favorable, as healing occurs in about 2 to 4 weeks. Occasionally severely affected bulls may develop adhesions between the penis and prepuce, or a stenosis of the prepuce may occur, possibly due to secondary infections. Scarring or adhesions of the vulva or vagina have not been reported.

Treatment is usually unnecessary and oftentimes is difficult to administer because of the problem of restraining the affected cattle due to the painful vulvar lesions. However, some authors recommend douching with mild antiseptics. Regular douching of the sheath of the affected bull with oily preparations might be indicated to distend the sheath and prevent adhesions. Breeding should cease for 3 to 4 weeks or until the affected animals recover. Because of its highly transmissible nature, this disease should be reported to the State Veterinarian. Veterinarians, inseminators, and others working in these herds should be careful not to carry and spread the infection. Vaccination with IBR vaccine is not indicated once the disease has appeared.

When IBR-IPV virus was present in semen used for intrauterine insemination of heifers it produced a necrotizing endometritis, short estrous cycles of 11 to 15 days in length, many cystic corpora lutea and only 1 of 12 heifers conceived.^{47,66} A number of practitioners have reported that low rates of conception occurred in heifers bred within one month of subcutaneous or intramuscular vaccination with an attenuated IBR vaccine. This has not been observed with the intranasal vaccines.

Specific Bovine Venereal Epididymitis and Vaginitis or "Epivag" is a chronic disease of cattle, transmitted by coitus and found only in East, South and Cen-

tral Africa. The cause is apparently a virus.⁵⁸ Vaginitis in cattle in South Africa may also be due to a viral agent similar to the IBR-IPV virus.^{30,56} The disease is characterized by a severe mucopurulent vaginal discharge in females, permanent adhesions of the Fallopian tubes, and by a hardening and swelling of the epididymis in the bull. This disease has been well-described.^{42,71,77}

Etiology—European cattle are very susceptible to the infection whereas Zebu cattle are resistant to the disease, at least, clinical symptoms are not exhibited. The disease has been transmitted experimentally by genital swabs from cow to cow or by placing minced infected epididymal tissue in the vagina. The material was bacteriologically sterile and no protozoa were found. The disease in the natural state is transmitted only by coitus. Preliminary attempts to produce the disease by filtrates of the material have failed. The disease is the most important cause of bovine sterility and infertility in Kenya.

In herds having breeding trouble 42 percent had this disease and in these herds 34 percent of the bulls became permanently sterile. The disease may remain latent in a herd for some time.⁷

Symptoms—The incubation period is 2 to 8 days. During the active stage of the infection there is an odorless, mucoid vaginal exudate, egg-white in consistency but opaque and yellow in color. The discharge from the vulva mats the hair on the tail and buttocks, forming dull, grey, yellow flakes as it dries. Speculum examination reveals diffusely reddened areas in the cranial portion of the vagina but there are no ulcers, vesicles, or granular lesions. A diagnosis of this disease in a herd is easy but in individual animals may be difficult. The acute infective stage may last for 2 weeks to 9 months. Estrous cycles are normal, but service is rarely followed by conception. In grade herds most cows and heifers recover eventually but 15 to 25 percent are permanently sterile due to unilateral or usually bilateral involvement of the uterine tubes with adhesions, hydrosalpinx, or ovarian and bursal adhesions.

In the bull a balano-posthitis may occur but it is mild and frequently not observed. The characteristic lesion in the bull is an enlargement and hardening of the epididymis that is usually bilateral. Although the entire epididymis is involved, the tail is involved most severely and may resemble a billiard ball in size and hardness. Occasionally an orchitis of a temporary nature may precede this epididymal enlargement and testicular degeneration and atrophy may occur. Bulls can be infected by intraurethral injection. The lesions in bulls take 3 to 6 months to develop and sexual desire remains normal. In advanced cases there are adhesions between the scrotum and the epididymis. On postmortem examination dry ad-

hesive areas of peritonitis or pleuritis may be found. The vesicular glands of bulls usually become enlarged and firm and changes may take place in the vas deferens.⁷

Treatment—The disease can easily be controlled by artificial insemination using noninfected bulls. In time it will spontaneously disappear from the females. More work is required on the determination of the etiologic agent, the length of time cows remain infected, and the practical methods of control when artificial insemination is not possible.

Miscellaneous Viral Infections of the Bovine Female Genital Tract

Contagious Anterior Vagino-Cervicitis in cattle has been described in South Africa as resembling the disease just described. However no permanent lesions are produced in the cow and no lesions are observed in the bull. The cause is not known.

An involvement of the uterus causing sterility as a sequela to lumpy skin disease of cattle in South Africa has also been described.^{77,79}

A catarrhal vaginitis and cervicitis clinically similar to "epivag" in cows was described in 4 herds in California.^{48,59} Affected cattle had a profuse nonodorous yellow mucoid discharge from the vulva. The cervix and vagina of the diseased cows was hyperemic and edematous but no pustules were present as in IPV. No other portions of the genital tract were involved. Although the disease appeared to spread following coitus, the bulls showed no clinical signs of the infection. The course of the disease lasted from 7 days to 3 months. Fertility was lowered and conception often was delayed several months. A few cows conceived during the clinical stages of the disease. The cause of this vagino-cervicitis was an entero-virus culturally different from the virus of "epivag." Sterility did not occur in this disease. Antibiotic treatments were of no value and immunity was short-lived.

Viral infertility in cattle has been characterized by a vaginitis, edematous endometritis, a mucopurulent genital discharge, abortions at 2 to 8 months of gestation with edematous fetal membranes, and by a temporary infertility in bulls.⁶⁰ The incubation period was 3 to 10 days. The disease could be spread to susceptible cattle by coitus and intravaginal, but not the intravenous injection of filtered genital mucus from infected cattle. It was reported that the virus, and possibly more than one was present, could be passed through eggs.

Transmissible viral fibropapillomas may occasionally be observed on the vulva and perineal region of heifers and the prepuce and penis of young bulls. The growths may be single or multiple. These tumors might be transmitted by coitus. The tumors in heifers are similar to the common skin wart and usually regress spontaneously in 2 to 6 months. This process may possibly be hastened by the use of wart vaccine. This condition does not cause infertility in heifers. The fibropapillomas may be removed surgically.³⁴

Bovine Virus Diarrhea (BVD)-Mucosal Disease (MD) virus is widespread in cattle. It has been incriminated in early embryonic deaths⁸ in cattle as well as in abortion, maceration, fetal mummification, congenital cerebellar disease and cataracts and other ocular defects. Seronegative cows for BVD-MD when bred naturally to a bull with semen containing the BVD-MD virus or given an interuterine injection of the virus after a natural service, all seroconverted within a few weeks but had a markedly reduced conception rate until this conversion occurred.^{57,81} No effect was observed in seropositive cows. Thus because most cows in the population are seropositive and BVD-MD virus is only rarely excreted in the semen, this virus is probably not a major cause of conception failure or repeat breeding.⁸¹

It has been demonstrated that BVD-MD virus may remain for weeks in the uterus and oviducts of cows. It has also been shown that BVD-MD virus causes no consistent lesions in the genital tract and no abnormalities of the estrous cycle occur as in IBR-IPV. But evidence has been presented that the BVD-MD virus may inhibit the normal development of preimplantation bovine embryos⁸⁻¹⁰ Further studies on the effect of BVD virus on developing embryos as a possible cause of repeat breeding is indicated.

Parainfluenza-3 virus infection given either intramuscularly or infused into the uterus after breeding had no effect on the breeding efficiency of infected susceptible heifers compared to control heifers not infected.¹⁹

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HORMONAL DISTURBANCES RESULTING IN INFERTILITY

Most hormonal disturbances causing infertility or sterility in cows and other animals are secondary to basic nutritional, hereditary and stress or work factors. Occasionally hormonal disturbances may be due to the ingestion or injection of exogenous steroids or other hormones. Hormonal diseases may include cystic ovaries, failure of estrum (anestrus) and repeat breeders due to failure of ovulation, failure of fertilization and early embryonic deaths. The widespread indiscriminate use of many hormones on an empirical basis by veterinarians 25 to 30 years ago has been followed in recent years by a much more selective and knowledgeable employment of the various hormones for their specific action in certain limited and carefully diagnosed infertility conditions. The use of assays for determining the plasma or milk progesterone levels further assists these diagnoses.

Cystic Ovaries

Cystic ovaries in dairy cattle is one of the most common conditions causing infertility, 6 to 19 percent,^{39b} that the veterinarian is called upon to treat. Twelve to 14 percent of all problem breeder cows have cystic ovaries.⁴⁹ A recent abattoir survey in England of 8071 bovine female genital tracts revealed that 10 percent had abnormalities. The most common abnormality was cystic ovaries with an incidence of 3.8 percent.³ In 5083 lactations over a 60 year period the percentages of dairy cows with cystic ovaries was 1.0, 3.1, 3.3, 4.0 and 5.2 for Brown Swiss, Ayrshire, Jersey, Guernsey and Holstein breeds, respectively.³⁰ In Holsteins the incidence of cystic ovaries for cows having twins was 12.7 percent compared to 4.9 percent for cows having single births. Cows with metritis had an incidence of 10.4 percent cystic ovaries compared to 5.1 percent of cows without metritis.³⁰ The more often the cow was treated for milk fever, the higher the likelihood that cystic ovaries would develop, 20 percent vs. 4 percent for cows with no milk fever. In 375 calving intervals in a Holstein herd cystic ovaries occurred in 11.2 percent. Seventy percent of the cysts occurred from 16 to 45 days after calving and 69 percent of these cows recovered without treatment and became pregnant prior to 300 days. Twenty-nine percent recovered in less than 30 days.³⁰ In 1599 Holstein lactations cystic ovaries occurred in 14.5 percent with the highest rate of occurrence 3.5 percent, or about 25% of cows with cystic ovaries, between 31 and 45 days postpartum. A second peak occurred in infertile cows after

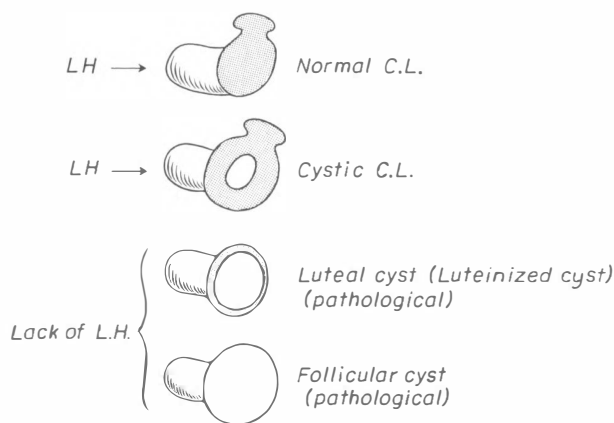


Figure 107. Cysts of the Bovine Ovary.

120 days.²¹ Thus in dairy herds cystic ovaries occur in 10 to 20 percent of problem breeders.³⁵ This latter review indicated that 10 to 40 percent of all dairy cows will develop cysts once in their lifetime and 35 to 45 percent of cows having one episode will have the condition repeated during their lifetime. Cystic ovaries occurred most frequently the second to fifth lactation.^{30,35,62} Since 60 percent of cows developing ovarian cysts before the first postpartum ovulation and 20 percent thereafter spontaneously reestablished estrous cycling,^{39b} the above estimates of the incidence of ovarian cysts are low. Thus cystic ovarian disease prolongs the postpartum interval to first estrus in 10 to 30 percent of dairy cows and is a serious cause of infertility.

Cystic ovaries in cattle are characterized by follicular cysts or cystic degeneration of the Graafian follicle, luteal or luteinized cysts, and cystic corpora lutea. Follic-

ular and luteal cysts are anovulatory cysts while the cystic corpus luteum is an ovulatory cyst. The basic cause for these cystic conditions appears to be a failure of the hypophysis to release sufficient amounts of luteinizing hormone, LH, to produce ovulation and proper luteinization of the corpus luteum. (See Figures 107 through 111.)

Follicular cysts are anovulatory follicles that persist on the ovary for 10 days and often much longer, have a diameter greater than 2.5 cm. and are characterized by either nymphomania or continuous or frequent estrus, or by anestrus. Luteal cysts are anovulatory follicles over 2.5 cm. in diameter that are partially luteinized and persist for a prolonged period and are usually characterized by anestrus. Follicular cysts and luteal cysts may be hard to differentiate clinically as there is great variation in the amount of luteal tissue in anovulatory cysts. The former may be multiple on both ovaries while the latter are more often single. The follicular cyst is thinner-walled and the wall is more tense and distended than the softer thicker-walled luteal cyst. The follicular and luteal cysts have a smooth convex surface since ovulation does not occur. The luteal cyst wall is thicker due to the presence of a lining of luteal tissue. The fluid in the luteal cyst is usually more amber or darker yellow or brown in color than the pale yellow clear fluid in the follicular cyst.⁷⁰ Follicular cysts are probably more common than are luteal cysts. Thirty percent of 1191 cystic ovaries contained luteal cysts,⁸⁰ (See Figures 107 through 111). Other workers have reported an incidence of 15 and 65 percent luteal cysts based on clinical examination and plasma progesterone assays.^{19,61}

Cystic corpora lutea follow a normal ovulation but contain a fluid-filled central cavity 7 to 10 mm. or more

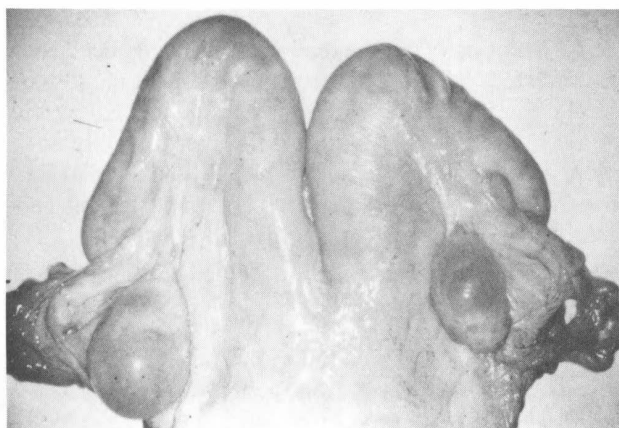


Figure 108. Cystic Ovaries in a Cow—bilateral follicular cysts with a flaccid atonic uterus.

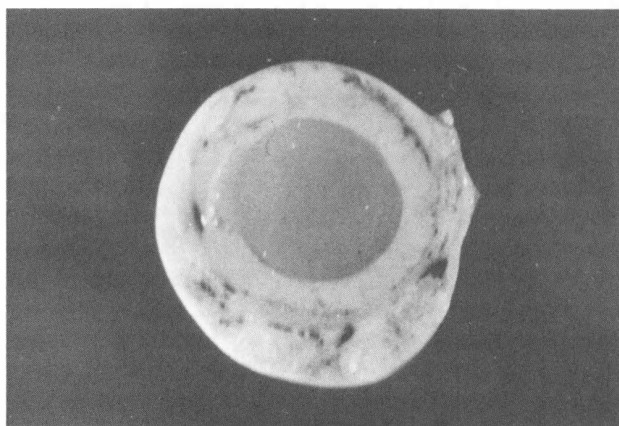


Figure 109. A Central Luteal Cyst in a Bovine Ovary.

(Courtesy K. McEntee.)



Figure 110. Bovine Luteal Cysts Associated with Superovulation following the Injection of FSH.

(Courtesy M. R. Jainudeen.)

in diameter. Cystic corpora lutea on rectal palpation feel similar to large, swollen normal corpora lutea as they have a projecting crown of luteal tissue that protrudes through the site of ovulation. Cystic corpora lutea often have a slightly fluctuating, soft consistency. This may be the most common of the cystic conditions affecting the bovine ovary with a possible incidence two and a half times greater than cystic follicles. Thirty seven cystic corpora lutea and 14 follicular cysts were found in 204 nonpregnant cows at slaughter.⁴⁷ In 357 estrous cycles followed by rectal examinations the incidence of normal corpora lutea, cystic corpora lutea and follicular cysts were 62.4, 25.2 and 12.3 percent.⁵⁴ The incidence of cystic corpora lutea was 34 to 41 percent in cycling

cows.^{20,29} The total progesterone in cystic corpora lutea was about 110 ug at 7 days of the cycle compared to about 180 ug in normal corpora lutea of the same age. About 100 to 150 ug of progesterone is needed in the corpus luteum to permit normal embryo development.⁶⁸ By 11 days of the cycle the cystic corpora lutea averaged 223 ug and the normal corpora lutea 295 ug of total progesterone.

Cows with cystic corpora lutea have normal estrous cycles and if conception occurs there is usually sufficient luteal tissue and progesterone to maintain pregnancy.²⁹ Small central cysts less than 7 mm. in apparently normal corpora lutea are common and may be found in up to 30 percent of corpora lutea.²⁶ These central cysts are lined by a layer of connective tissue, they become smaller late in the estrous cycle as the corpus luteum regresses and are seldom found in pregnant cows' corpora lutea after the fourth or fifth month of gestation.^{26,47} For practical purposes most cystic corpora lutea are not pathological; ovulation was normal; they do not influence cycle length;^{47,54} they may follow a slightly longer than normal estrous period;⁴⁷ and most cows with cystic C.L. usually maintain the pregnancy to term. However, they may be caused by mild faulty release of L.H. hormone and thus be caused by the same basic deficiencies producing follicular cysts and luteal cysts.^{26,47,67}

Since cystic corpora lutea have a questionable pathologic significance the term cystic ovaries will be applied only to the common follicular cysts and less common luteal cysts. Further detailed clinical, histological and endocrinological studies are needed to more accurately assess the incidence of each type of cyst since recent reports have indicated the incidence of luteal cysts to range from 15 to 70 percent and follicular cysts from 30 to 85 percent.^{19,35,61,80}

Etiology—Cystic ovaries is principally a disease of all breeds of dairy cows although occasionally beef cattle are affected. While the author has observed the disease most often in Holstein cattle, it must be pointed out this is the major breed in New York State. The disease is more common in closely-confined, stabled animals during the winter months of December, January and February, than during the summer and fall months.^{32,54,62} The latter authors reported 44 and 48 percent of their cases of cystic ovaries occurring during these three months. However in New York State there is a concerted effort to have cows calve in the fall of the year. Cystic ovaries affects cows of all ages from puberty to senility but is most commonly observed following the second to the fifth parturition,^{24,30} or from 4-1/2 to 10 years of age.³² In 295 cases studied by the author⁶² 41, or 13.9 percent, occurred in cattle from 1 to 3 years of age; and only 3

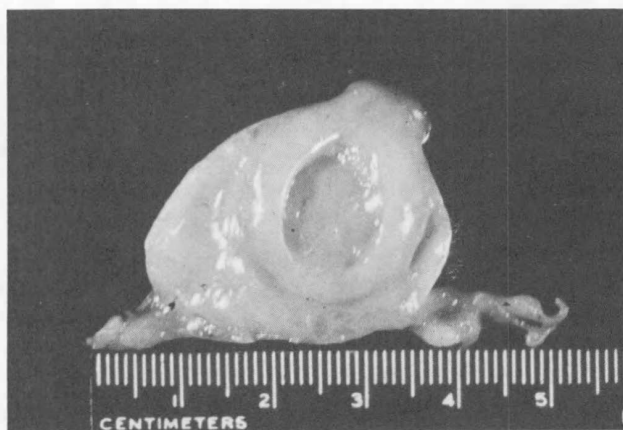


Figure 111. A Bovine Cystic Corpus Luteum.

(Courtesy K. McEntee.)

of these were virgin heifers; 160 or, 54.2 percent, occurred between 4 and 6 years of age; 74, or 25.1 percent, between 7 and 9 years of age; and 20, or 6.8 percent, over 10 years of age. In a study of 64 cystic cows in a herd of 341 head over a period of 10 years the number of cows that developed cystic ovaries in any given service period after the first period was fairly constant.¹² Certain cows may have repeated attacks of cystic ovaries during a service period or during different service periods. Of 433 cows studied 53 suffered repeated attacks.²⁴ In 341 cows 64 cows had cystic ovaries; of these, 12 were affected at 2 service periods, 4 at 3 service periods, and 2 at 4 service periods.¹² Thirty-five to 45 percent of cows with cystic ovaries had repeated attacks within a service period.³²

The occurrence of cystic ovaries is closely associated with stress in the periparturient period. Twin births, retained placenta, metritis and milk fever were associated with an increased incidence of cystic ovaries.^{30,54,55} The high incidence of the occurrence of cystic ovaries between 15 and 45 days postpartum coincides with peak levels of milk production and the onset of estrous cycles.^{21,78} ACTH, 200 IU given intramuscularly near estrus prevented the LH surge and estrus in 5 of 6 Holstein heifers.⁶⁹ ACTH, 300 IU given daily during the follicular phase, from about day 16 of the estrous cycle caused ovarian cysts in nonlactating Holstein cows.⁴³ Thus stress-induced ovulation failure may be a cause of spontaneous follicular or luteal cysts. It is seen more commonly in the higher producing cows. Affected cows have a higher quantitative milk yield than do normal cows. On the basis of the average milk yield in the herd, 45 percent of the nymphomaniac cows were excellent producers, 48 percent fair producers and only 7 percent poor producers.^{12,24} The occurrence of nymphomania was not associated with the level or percentage of butter fat produced. There were 1280 service periods, 341 of which were in virgin heifers, during which the animals were not milked; 457 records were made during the time the cows were in the milking herd and milked twice daily, and 105 records on animals started on test but returned to the milking herd before conception; and there were 359 service periods of cows on official test being milked 3 or 4 times a day.¹² In these 4 categories the incidence of nymphomania or cystic ovaries was 3.4 percent, 6.8 percent, 8.5 percent and 10.6 percent, respectively. The increased incidence of cystic ovaries in test cows might be explained either on higher production, increased feeding, more frequent daily milking, or all three factors.¹

Many workers believe that increased feeding especially of rations high in protein stimulate lactation and the development of cystic ovaries. This fact could not

be confirmed but the evidence was suggestive.⁵⁷ The time of onset of cystic ovaries in cattle is usually from 1 to 4 months after calving, with a peak around 15 to 45 days.^{21,45,54,78} This is the time when milk production is usually the highest. This condition may occasionally occur following repeated services as late as 4 to 9 months after calving.^{21,61} Nymphomania or cystic ovaries occurred even in heifers that were withheld from service for a number of years.¹⁷

In 312 cases of nymphomania or cystic ovaries observed by the author there appeared to be a seasonal incidence of the disease; 151 cases, or 48.4 percent, occurred during the months of December, January and February. During these same months in comparable years the N.Y. State Artificial Breeders Cooperative inseminated only 35.7 percent of over 325,000 cattle bred those years. High feeding levels causing increased milk production, coupled with lack of exercise and sunlight might be contributing factors to the cystic condition during the winter months.^{54,62}

There is evidence to show that nymphomania or cystic ovaries is hereditary. This conclusion has long been held by clinicians. A hereditary predisposition to nymphomania existed in the Swedish Highland breed.²⁴ In 331 Swedish Red cattle affected with nymphomania, 26 percent of their dams had nymphomania, 41 percent were normal, and in the remainder this information was not known. In the Friesian breed 102 cows had nymphomania and of these 21 percent of their dams had nymphomania, 45 percent were normal, and in the remainder no information was obtained.²⁴ Of 245 daughters out of 144 dams 43 dams had been cystic; they produced 82 daughters, of which 26.8 percent developed nymphomania.¹² The remaining 101 dams had never been cystic; they produced 163 daughters, of which only 9.2 percent developed cystic ovaries. In their data there was no evidence of an heritability of cystic ovaries from cows staying in the herd for less than 4 service periods. They therefore eliminated those cows and recorded only those that remained in the herd for 4 service periods or more. Dams with cystic ovaries had 27 daughters, of which 48.1 percent had cystic ovaries whereas noncystic dams had 46 daughters, of which only 21.7 percent had cystic ovaries. Nearly all cows that suffered from a recurrent development of cystic ovaries had a genetic predisposition to the disease.³² Because of this factual evidence and the many observations by most practicing veterinarians of cystic ovaries in succeeding generations of a cow family, there is every reason to assume the existence of a hereditary predisposition to cystic ovaries and nymphomania. In recent years, with the increased use of artificial insemination and the increased level of pro-

ductivity in our purebred and commercial dairy herds, the incidence of this condition is increasing. In a few herds the problem of cystic ovaries became so severe that the owner became discouraged and the herd was dispersed.³¹ In the Ambulatory Clinic of the N.Y. State Veterinary College the incidence of cystic ovaries rose from 333 cases between 1948 to 1953, to 1530 cases between 1963 and 1968—or over a 100 percent increase for each 5 year period in an area where cow numbers declined slightly from 1943 to 1968. Some of this increase may be due to the farmer becoming educated, recognizing the symptoms and calling for treatment: or preventive herd health practices including routine postpartum examinations of the genital organs may result in earlier diagnosis and treatment with fewer cases of spontaneous recoveries occurring.⁷⁸ It may be because treatment is usually successful in maintaining the cow in the herd so that the condition may recur subsequent years; or it may be due to widespread use of bulls by artificial insemination that transmit this inherited predisposition toward cystic ovaries along with high milk production.

Further study should be made of the heritability of this condition. A significant sire line effect on the incidence of cystic ovaries in a large purebred Holstein herd was noted.⁵⁰ In a recent report of 2,112 calvings over a 7-year period by 649 cows in one dairy herd 17 percent of the cows produced at least one daughter that had cystic ovaries. Two bulls sired 17.6 percent of these affected daughters significantly more than was expected since they sired only 11.6 percent of all the daughters in the herd.^{42b} In Sweden where AI bulls siring daughters having a higher than normal incidence of cystic ovaries were culled the frequency of cystic ovaries declined from 10.8 percent in 1954 to 5.1 percent in 1961.⁴ Also the two abnormalities of ovulation, cystic ovaries and twinning, are closely associated and both are probably hereditary. The relationship was discussed in Chapter IV. AI studs in the United States should heed with concern and action the above evidence.

The actual mechanism leading to the development of cystic ovaries is not completely understood. The discovery that injections of gonadotropic substances rich in L.H. had a highly specific and curative effect on this condition, definitely indicated that the disease was probably due to a deficiency of LH hormone normally released prior to the time of ovulation.¹³ The delta cells of the anterior pituitary that produce gonadotropic hormones degranulate or release their hormone shortly after the onset of estrus in normal cows. In cows that fail to ovulate this degranulation fails to occur, or may occur later, or may not occur as completely as in normal animals.^{37,48} Pituitary gland gonadotropin content at estrus and four

days after normal estrus and ovulation was 3.0 to 9.1 ug while in cows with follicular cysts, the pituitary glands contained 6.1 to 15.1 ug of gonadotropin at estrus and 4 days later.²⁰ Thus in cystic ovaries the normal release of LH failed. The failure of the release mechanism or an actual deficiency of luteinizing hormone from the anterior pituitary gland prevents normal ovulation and development of the corpus luteum. Since in cows with cystic ovaries plasma levels of estradiol, progesterone, FSH and LH and testosterone were the same as found in the various stages of normal estrous cycle, evidence would indicate that the cause of cystic ovarian disease is due to an abnormal time sequence of hormonal changes rather than differences in the concentration of the hormones between cystic and normal cows.¹⁹

In a series of 5 cases treated by the author⁶² one dose of LH was given to each cow after a normal estrous cycle and estrum followed by continuous symptoms of nymphomania, 2, 5, 5, 6, and 7 days and the presence of cystic follicles. These cows conceived to the insemination or natural service on the first day of estrum preceding the development of the nymphomaniac symptoms. This probably indicates that enough L.H. was present to cause ovulation but not enough to cause normal luteinization of the follicle with the result that a number of other follicles matured, failed to ovulate and became cystic. The injected luteinizing hormone caused a rapid luteinization soon enough so that normal attachment and development of the fertilized ovum took place. If treatment had not been given, the fertilized ovum probably would have perished and a well-established case of nymphomania or cystic ovaries would have developed. Others have recorded similar cases of cystic ovaries treated within 10 days after insemination and fertilization in which pregnancy occurred from that service.

Cystic ovaries in cattle can be produced by the injections of estrogens, especially in the latter third of the estrous cycle.²³ Intramuscular injections into cycling cows of doses greater than 4 mg. of estradiol or 40 mg. of stilbestrol may result in cystic ovaries. Prolonged or high doses of estrogens have been reported^{15,16,47} as causing cystic ovaries. Androgens could also cause this disease. Thus exogenous injection of steroids and possibly other hormones can interfere with the normal release of L.H. and produce cystic ovaries. Cystic ovaries were produced experimentally^{58a} by the injection of 5 mg estradiol benzoate on day 16 of the bovine estrous cycle or the injection of bovine LH antiserum before the onset of estrus. The former injection caused premature release of LH and resulted in smaller cysts, 2 to 3 cm., than the latter treatment, 5 to 6 cm. cysts. In both types of cysts the plasma estrogen levels were elevated. Thus cystic

ovaries may be due to premature release of LH or an insufficiency of LH at the time of ovulation.

A hyperestrogenic syndrome in unrelated dairy cattle in Israel characterized by cystic ovaries, udder development in calves, increased incidence of estrus during early pregnancy, estrogenic changes in the genital organs, infertility, and abortions caused by feeding large amounts of alfalfa hay with a high estrogenic content was described.² Estrogens might also be present in higher than normal amounts in red clover, pea ensilage and mold on hay and silage.¹ If a herd experiences more than a 30 percent incidence of cystic ovaries and hereditary factors are not the cause, estrogens in the feed should be suspected.^{5,8,38}

The pituitary gland and especially the adrenal gland were larger in cows with cystic ovaries than in normal cows. Certain cows with cystic ovaries exhibited a masculine behavior and appearance and had increased levels of 17-ketosteroids from the adrenal gland in the urine.²⁴ This syndrome was called "adrenal virilism." However, the bovine adrenal gland is a poor source of androgens.⁶⁷ Many long-time nonlactating sterile cows develop a steer-like appearance.

The steroid content of ovarian cysts was studied and the previous literature was reviewed.⁶⁷ Although estradiol-17B was the major steroid in normal ovarian follicles, the concentration of this steroid was significantly lower in follicular cysts, 50 to 75 ug. vs 20 to 30 ug. per 100 ml. of fluid, respectively. Histologically the steroid producing granulosa cells in the follicular cysts were undergoing atresia. Some cyst fluid samples contained large amounts of progesterone and these cysts on histologic examination showed atretic or luteinizing changes. Other steroids such as estrone and androstenedione were also found in the cyst fluids. The absolute concentrations and relative amounts of various steroids found differed greatly both between animals and within the same animal. There was no correlation between the size of the cyst and the hormone content. The cyst itself was not the primary defect in ovarian disease.⁶⁷ Cysts were degenerating structures both histologically and endocrinologically. In normal follicles growth and endocrine activity accompanied each other while in cysts follicular growth continued but endocrine activity declined. Neither the concentrations or the total amount of estradiol indicated the cysts produced increased amounts of estrogen. However, estrogens were produced in cystic ovaries for a longer period of time and more continuously than estrogens in a normal cycling cow.

It was impossible to correlate the behavior exhibited by cystic cows with the steroids present in the cysts. This behavioral pattern was complicated since both proges-

terone and testosterone can potentiate estrogens in bringing a cow into estrus. Progesterone in large doses can inhibit estrus in an estrogen-primed animal. Cows tend to become refractory to even high doses of estrogen and fail to show signs of estrus. Furthermore the frequency of the development of new follicles and hormonally active cysts will affect the behavior of the cystic cow.⁶⁷

In 23 cows with cystic ovaries, 21 had estradiol plasma levels higher than those recorded during the preovulatory surge of estrogen in normal cows, 25 to 100 pg/ml. While 11 cows had plasma levels of progesterone over 1.5 ng/ml, commonly seen in normal cows in diestrus. The presence of progesterone in these cows did influence the estradiol levels.⁶⁴ Eight cows with ovarian cysts were studied over 30 days and LH plasma concentrations were different within and among the cows. Only one cow had a mean progesterone level above 1.0 ng/ml, but concentrations greater than this were observed in at least one of the samples in the other 7 cows during this period. With the development of new cysts, older cystic structures regressed in 6 of the cows but no spontaneous recoveries occurred during this period in the 8 cows.³⁹ The presence or absence of behavioral estrus, nymphomania or anestrus could not be associated with the endocrine levels in the blood plasma.⁶⁴ The concentrations of estradiol, progesterone and testosterone from non-luteinized vs luteinized bovine ovarian cysts were 81.9 vs 3.5, 163.7 vs 563.4, and 4.4 vs 2.1 ng/ml, respectively.^{32b} The concentrations of estradiol, progesterone and testosterone in normal follicular fluid and ovarian cyst fluid about 10 days after treatment with 100 ug GnRH causing luteinization of the outer cells of the theca interna^{10b} were 55.7 vs 3.9, 181.9 vs 766.0 and 5.7 vs 3.0 ng/ml., respectively.^{32b}

Thus physical changes in cystic structures together with the development of new cysts in the ovaries, variations in the hormonal content of the ovarian cystic fluid⁶⁷ and changes and variations in the level of estradiol, progesterone and LH in the blood plasma of cows with cystic ovaries indicate that the condition of ovarian cysts is not a stable or static but a changing one. Follicular cysts may become luteal cysts. Older luteal or follicular cysts may involute and disappear when new follicles and new cysts develop.³⁹

Some older authors and veterinarians indicated that cystic ovaries were associated with or even due to uterine infections. The uterus was examined histologically and bacteriologically in 62 cows with cystic ovaries and evidence of an endometritis was found in only 4 cases. Infection of the uterus is seldom seen associated with cystic ovaries. Of the author's cases of cystic ovaries or nymphomania, 72 cows conceived promptly within 60

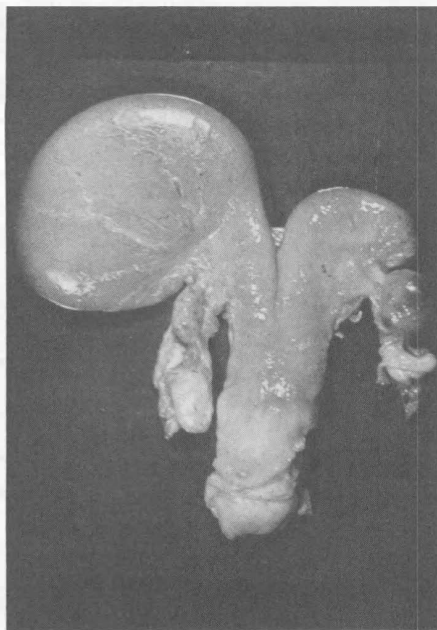


Figure 112. A Chronic Cystic Ovary Associated with a Unilateral Mucometra.

Courtesy K. McEntee.

days of treatment without treatment of the uterus. A few cases of infection were encountered.

Signs—Cystic ovaries develop in cattle most commonly from 15 to 45 days postpartum.^{21,45,54,78} but may occur quite commonly up to 120 days or more. Behavioral signs are variable for several reasons as discussed under the etiology but for general purposes cows can be divided into two groups, nymphomaniac and anestrus cattle. The cows with nymphomania exhibit frequent, irregular, prolonged, or continuous signs of estrum. These cows are often nervous, restless, and bellow frequently. Only very rarely does a nymphomaniac cow become vicious. These cows may occasionally accept the riding of another cow, or coitus by the bull at any time. Most nymphomaniac cows frequently attempt to ride other cows but often refuse to stand to be ridden. Nymphomaniac cows may be as sexually aggressive as a bull in seeking out and attempting to mount a cow approaching or in estrum. The homosexual and heterosexual characteristics of cattle are aggravated during this disease. The affected cows because of their actions are often spoken of as “bullers.” These cows, especially if on pasture are likely to lose weight during the disease because of constantly moving about, attempting to mount, and stirring up the other cows. The cows with the cystic ovaries that show anestrus are not observed in estrum for long periods of

time, several months or more. In this group of cows the symptoms of estrum, if they are present, are very mild and infrequent. The owner of these cows, if they have been bred, may believe them to be pregnant. Others, about 15 to 20 percent, have had a normal estrum or two and then failed to show estrum thereafter even though they were not bred. Some of these cows may at times act as if they might be in estrum but refuse to stand for the bull or for other cows to mount them. Some cows with cystic ovaries may show anestrus initially and then exhibit nymphomania later or conversely some nymphomaniac cows may continue to have cystic ovaries but after a varying period of time exhibit anestrus.

The incidence of cows with cystic ovaries exhibiting nymphomania or anestrus varies and is strongly influenced by the postpartum interval at which the condition is diagnosed per rectum. More cystic follicles developed from 0 to 30 days than from 31 to 60 days postpartum. About 85 percent of the cows, that developed follicular cysts prior to 60 days exhibited anestrus.^{45,55} A study of 187 cows with cystic ovaries in which many were examined in the early postpartum period of 30 to 60 days reported a 62.5 percent incidence of anestrus.⁹ A study of 265 cases of cystic ovaries examined only at the request of the owner from about 80 to 150 days after calving reported the incidence of anestrus to be 26.4 percent.⁶² Thus as the number days following calving at which the cystic ovarian condition is diagnosed increase the incidence of nymphomania also increases.

A constant and prominent sign of cystic ovaries is the relaxation of the sacrosciatic ligament, most noticeable at its caudal border.²⁴ In cows showing nearly constant estrum 78 percent of the cows had highly relaxed ligaments, 10 percent moderately relaxed and 6 percent slightly relaxed ligaments. In cows with frequent heats, 50 percent had highly relaxed 42 percent moderately relaxed and 5 percent slightly relaxed ligaments. In a few cases because of the relaxing effect of estrogens on the pelvic ligaments constant mounting and being mounted may lead to dislocation of the hips and to pelvic fractures. The pelvic ligaments of anestrus cows were highly relaxed in about 40 percent of the cows, moderately relaxed in 30 percent, slightly relaxed in 12 percent and normal in 18 percent of the cows. The genital organs are usually slightly edematous and atonic. The vulva is often increased in size, and relaxed and swollen. Prolapse of the vagina and symptoms of pneumovagina may occur especially in nymphomaniac cows. An increased amount of mucus may be present and appear as a discharge at the vulva. This mucus is thicker, more tenacious, and more opaque than the mucus of estrum. The mucus is whitish grey in color, giving it the appearance of a mu-

copurulent discharge. However there are usually few leucocytes in the mucus. The external os of the cervix is usually large, dilated, and relaxed.

On rectal examination the relaxation of the pelvic ligaments is very noticeable on palpation. The cervix, especially the external os, is usually large, and the uterus is also enlarged, and its walls are thickened and flaccid. In long-standing cases of cystic ovaries the uterus may be atrophied, small and flaccid. On palpation of the uterus it seldom develops tonicity or becomes erect or turgid as usually occurs in a normal uterus especially at or near estrum. One or 2 to 4 cysts varying in size from 2 to 7 cm. in diameter are felt on one or both ovaries. These cysts are usually peripheral in location, thin-walled and burst readily with pressure applied by the fingers. At times it may be difficult to differentiate between a cyst and a normal follicle. Cysts persist for 10 days up to several months or longer. No luteal tissue or corpus luteum is usually palpable in the ovaries of cows with follicular cysts. Even cystic corpora lutea are not present. Occasionally a thick-walled, rather fluctuating, luteal or luteinized cyst may be found. These are often associated with anestrus cows. Occasionally a large atretic follicle together with a normal corpus luteum may be found in a pregnant cow the first trimester of gestation. This does not affect the pregnancy. Usually the cyst is larger than 2 or 2.5 cm. in diameter whereas the normal follicle is smaller. The cyst is usually thicker-walled than is the follicle. The uterus of a cow with cystic ovaries is usually flaccid, whereas the uterus during estrum is erect and tonic. The mucus of estrum is much clearer and more stringy than that in the cow with cystic ovaries. Occasionally cows 40 to 90 days pregnant may have a good-sized follicle and a normal corpus luteum. A cyst larger than 8 to 10 cm. in diameter may indicate the presence of a granulosa cell tumor.

The size and number of ovarian cysts were similar for both nymphomaniac and anestrus cows.^{24,62} The incidence of ovarian cysts in 433 cows was as follows: both ovaries cystic 50 percent, right ovary cystic 31 percent, and left ovary cystic 19 percent.²⁴ The author in a total of 352 cases found the incidence to be 43.8 percent, 33.2, and 23 percent, respectively. On postmortem examination of the genital organs of 6286 Swedish Highland cows an incidence of 14.8 percent cystic ovarian degeneration was found, 6 percent involved only the right ovary, and 5.5 percent involved both ovaries. Thus in nymphomania, as in the incidence of left- and right-horn pregnancies, the fact that the right ovary of cows is slightly more active or functional than the left is further illustrated.

Gross examination of cystic ovaries revealed the fact that multiple cysts were more common than were single

cysts and the large single cysts frequently showed evidence that they had been formed by the union of several cysts.²⁴ The lining of the cyst was smooth and basal portions occasionally had a thin circumscribed area of yellowish lutein tissue. Some lutein tissue has been observed in many ovarian cysts by the author and his associates. The cystic fluid was clear and slightly yellow or amber in color. In large cysts the ovarian tissue was atrophied. On histologic section the granulosa layer of cells and ovum are often missing, but scanty portions of granulosa cells could be found in the basal portions of the cyst and in some cases these appeared luteinized. The theca interna was likely to be flocculent and edematous and show degenerative changes. Some hyaline changes in the theca interna were occasionally observed. The degenerative changes were more marked in the peripheral portions of the cyst.²⁴

The gross appearance of the uterine tube was normal in most cases.²⁴ Sometimes the uterine tube was thickened and some yellow fluid could be squeezed out after incising it. Microscopically this was composed of epithelial cells and debris. In cows with cystic ovaries the ovarian bursa or ventricle was larger than normal and the mesometrium was more relaxed. In nymphomaniac cows the uterus and cervix usually were large, edematous, and flaccid. The cervical canal was dilated and relaxed, permitting a finger or pencil to pass through. The endometrium was smooth, moist, semi-transparent, and edematous. In a few cases cystic enlargement of the endometrial glands was noticed as pinhead rounded elevations with transparent capsules. Usually the uterus was empty but the endometrium was covered with thin mucus. Occasionally as much as 100 ml. of mucus was found in the uterus. The vagina, clitoris and vulva were swollen. Microscopically the greatest changes are found in the uterine mucosa. These changes, especially in nymphomaniac cows, were characterized by marked hyperplasia of the mucosa and cystic dilation of the endometrial glands. In some cases cystic dilation was so marked that the endometrium developed a typical Swiss-cheese appearance on histologic section. (See Figure 113.) In some anestrus cystic cows with a small uterus the mucosa showed slight atrophic changes and hyperplasia and cystic dilation of uterine glands. These hyperplastic and cystic changes in the endometrium are characteristic of changes produced by long-continued action of estrogens from the cystic ovaries.

In long-standing cases of nymphomania the relaxation of the pelvic ligaments produces a tipping of the pelvis and an elevation of the tail head that is made more pronounced by the relaxed sacroscopic ligaments. This elevated tail head is sometimes called the "sterility hump"

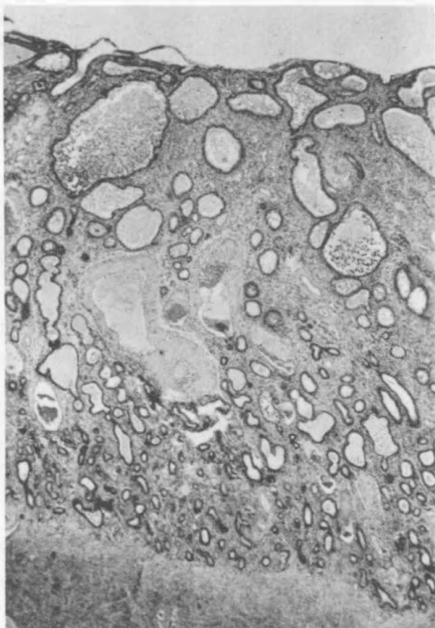


Figure 113. Cystic Endometrial Glands Caused by Cystic Ovaries.
Courtesy K. McEntee.

because it tends to persist after recovery. (See Figure 114.) Associated with the elevation of the tail head is the elevation of the ischial tuberosities and a ventral dropping of the lumbosacral articulation. This tipping of the pelvis may result in an unsteady gait and a predisposition to injury. These changes in the pelvic ligaments are associated with prolonged low level estrogenic stimuli and probably not due to excessively high estrogen levels in the blood plasma.¹⁹



Figure 114. A "Sterility Hump" in a Cow Associated with Chronic Cystic Ovaries and Relaxed Pelvic Ligaments.

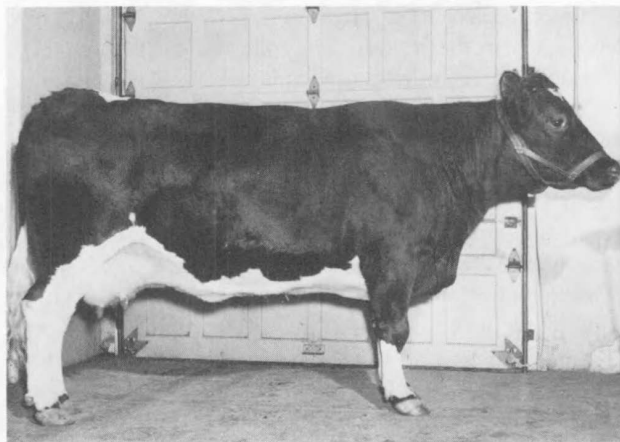


Figure 115. A Steer-like Appearance of a Cow with Chronic Cystic Ovaries and Infertility Lasting for Three Years.

Hydrometra or mucometra may develop following a long-standing condition of cystic ovaries. (See Figure 112.) Cows with cystic ovaries observed by the author and his associates were initially treated apparently successfully and bred. The owners believed them to be pregnant but after 6 to 8 months the normal signs of pregnancy did not develop. Rectal examination revealed mucometra and cystic ovaries. A marked atrophy of the uterine wall or myometrium had occurred with severe cystic dilation of the endometrial glands resulting in mucometra with the uteri containing 100 to 1000 ml. of watery mucus. (See Figure 113.) On rectal examination in some cases the uterine wall was found to be so thin that it was difficult to palpate. Hydro- or mucometra may affect only one uterine horn or a portion of one horn. The ovaries were usually larger than normal but the cysts were multiple, small (1 to 2 cm. in diameter), and thick-walled. The cysts were extremely difficult or impossible to rupture by manual pressure. This same condition occurred in 3 heifers that developed chronic cystic ovaries out of 25 heifers that were withheld from breeding for 4 to 5 years.¹⁷ The cervical canal in these cases is usually closed by an accumulation of mucus and debris. In one case in which treatment was instituted by the author to relieve the mucometra by drawing off the mucus, infection was established and pyometra resulted. In another cow with 100 ml. of mucus in the uterus, 20,000 I.U. of chorionic gonadotropin was injected intravenously and luteinization of the cysts and expulsion of the mucus from the uterus resulted. Most cases however fail to respond to treatment. The marked similarity of this condition in cattle to cystic degeneration of the uterine wall in horses, and to hyperplasia of the endometrium with cystic di-

lation of the endometrial glands, hydrometra, and, in some cases, secondary pyometra in dogs is evident. The endometrial changes are probably produced in the three species by the gonadal steroids, estrogen and/or progesterone.

In rare cases of chronic cystic ovaries and anestrus the cervix may become greatly enlarged to 5 to 6 inches in diameter and filled with a tenacious mucus, mucocervix. The uterus in these cases is flaccid but not distended with mucus. The cause and prognosis are similar to mucometra.

The effect of cystic ovaries on milk production is variable. Some authors report a drop in milk production in nymphomaniac cows. Others report good milk production until treatment is given, at which time there is a drop in production. In a careful study of 74 cows it was demonstrated that the cystic condition was apparently responsible for increased production.³⁶ The longer the cows were cystic the greater the production of milk. Cows with anestrus produced more milk than nymphomaniac cows. This indicated that the low levels of estrogen from the cystic ovaries probably stimulated milk production.

Prognosis—The earlier that cystic ovaries are diagnosed and treated, the better is the prognosis. In a series of 229 cases diagnosed and treated by the author within 6 months of parturition 79 percent conceived after 1 treatment, 10.7 percent had to be retreated, and 10 percent were sold because they were sterile, poor producers, or for other reasons. In 46 cows diagnosed and treated between 6 and 12 months after calving, although 78.3 percent recovered, only 58.7 percent conceived after one treatment and were retained in the herd, 8.7 percent were retreated, and 32.6 percent were sold. Many were sold because it was not economical to maintain them as non-lactating cows for many months in commercial herds. There was no essential difference between the rate of recovery and conception rates between cows showing nymphomaniac symptoms and cows showing anestrus. In 124 cases of nymphomaniac cows treated within 60 days of the onset of symptoms 78.2 percent conceived and 21.8 percent were sold. In anestrus cows, symptoms in many cases were lacking or unnoticed for an undetermined period of time. Of 46 cows, many of which had not been observed in estrus since calving, treated within 120 days of the onset of anestrus, 76.1 percent conceived and 23.8 percent were sold. The size or number of the cysts bore no relation to the symptoms shown or to the rate of recovery. In some cases two or more treatments may be necessary to effect a cure. Recovery is not assured until the affected cows are safely pregnant. About 20 to 30 percent or more of cows with cystic ovaries if they conceive will develop cystic ovaries again at

subsequent service periods. Another factor to be considered seriously in the prognosis is the possible furthering of this cystic problem to the future detriment of dairy breeds inasmuch as there is a definite hereditary predisposition to cystic ovaries and twinning. Cows having two or more episodes of cystic ovaries were hereditarily predisposed toward the disease.^{32a} Bulls with an increased incidence of daughters with cystic ovaries should be slaughtered.^{4,32a}

The prognosis in cases of severe cystic degeneration of the endometrium and atrophy of the uterine wall in hydrometra or mucometra is poor. Most cows with mucometra or rare cases of mucocervix should be sold since only a very few cases respond to treatment. Spontaneous recovery from cystic ovaries frequently occurs. About 50 percent of the cases of cystic ovaries occurring within 45 days of calving recovered spontaneously before 60 days postpartum. In 42 cows with cystic ovaries, 30 of which developed between 15 and 45 days postpartum, 69 percent recovered without treatment and became pregnant before 300 days postpartum.⁷⁸ In 34 cows treated for nymphomania about 15 percent were sold as sterile and the remainder required about 3 services per conception after treatment; about 40 percent of the cows conceived on first service.⁷³ A lowered conception rate associated with early embryonic deaths following recovery from cystic ovaries was also noted.⁵⁰

Treatment—Rational treatment should have as its aim the development of a functional normal corpus luteum either by spontaneous recovery or rupture of the cysts, repeatedly if necessary, administration of GnRH or luteinizing hormone (LH) or preventing the continuous release of luteinizing hormone from the pituitary gland by the administration of progestational compounds. The bovine corpus luteum is formed mainly from the granulosa and thecal cells.⁶⁷ Since these cells are the first cells to degenerate in the cystic follicle, treatment to be successful should be undertaken soon after cyst formation or when newer young cysts are forming on the already cystic ovary containing follicular or luteal cysts.

The earliest reported treatment for cystic ovaries consisted of repeated manual removal or rupture of the cysts at 6- to 10-day intervals until a normal cycle and corpus luteum developed. This frequent manual massage and trauma to the ovary is not desirable if it can be avoided; moreover, repeated visits by a veterinarian for the massage of the cow's ovaries is costly. In a series of 188 cases reviewed by the author in which cystic ovaries were treated by manual removal of cysts, a recovery rate of 37.2 percent was reported.^{14,51,62} Of 24 cases of cystic ovaries occurring in a herd of 150 cows, 8, or 37.5 percent, conceived twins after treatment.¹⁴ Of 11 animals

bred within 35 days after removal of the last cyst, 6, or 54.5 percent, conceived twins; only 3, or 24 percent, of 13 animals bred after 35 days following rupture of the last cyst had twins. Because of this high twinning rate following treatment it was then recommended that breeding be deferred until the second normal estrum unless the ovaries were palpated to determine the presence of 1 or 2 ripe follicles, and the cow then bred or not bred accordingly. In cows having ovarian cysts centrally located, or thick-walled so that manual rupture was not possible, the treatment required tapping the cyst with a needle or ovarian scalpel through the vaginal wall. Stoll's cyst aspirator⁷⁰ works well in these cases. Two hundred forty two cows with cystic ovaries were treated by manual rupture of the cysts. Three-quarters of these cases were treated within three months of parturition. Cows with the shortest time interval from parturition to treatment recovered significantly more quickly; 45.7 percent or 107 cases, recovered after one treatment.⁶⁵ These results complement the observation that single ovarian follicular cysts occurring before 45 to 60 days after calving have a 50 percent spontaneous recovery rate and the observations of many veterinarians that manual removal of these early postpartum cysts is often successful in restoring a normal sexual cycle.⁵⁴ Many veterinarians may manually remove cysts prior to 50 days but do not treat with LH or GnRH until 50 to 60 days or more postpartum. A trial on the comparative efficacy and costs of spontaneous recovery of early ovarian cysts, manual rupture of these cysts which usually is easily accomplished, and treatment with GnRH or HCG should be conducted on cows in which ovarian cysts are diagnosed prior to 60 days postpartum. Spaying will correct nymphomania but removing only one ovary if it is affected with cysts is useless, since the remaining ovary will promptly develop cysts. Affected nymphomaniac cows should be kept isolated from the herd so that they do not annoy or injure themselves or other cattle by excessive mounting.

Although a number of authors had suggested the possible value of LH in treating bovine cystic ovaries and the successful treatment of a few cases with LH ("Antuitrin S") in 1943 was reported,⁸ it was not until 1944 that successful results in the treatment of many cows with cystic ovaries, both follicular and luteal cysts, using unfractionated sheep pituitary extracts intravenously was published.¹³ This report demonstrated the value of LH in curing the disease. Of 81 cows with nymphomania or cystic ovaries treated, 88 percent recovered and had a normal corpus luteum in 31 days. Of 53 cows bred after a single injection of the pituitary extract, 36 conceived. After retreatment of 16 animals 6 more became preg-

nant. Thus a total of 68 percent conceived. These workers reported that it was not necessary to rupture cysts prior to treatment. Since then a number of reports on the treatment of cystic ovaries have recorded the successful use of pituitary extracts rich in LH, or chorionic gonadotropin HCG.⁶²

Injections of human chorionic gonadotropin (HCG) 5000 I.U. intravenously and 10,000 I.U. intramuscularly resulted in a higher incidence of conceptions than 2500 I.U. intravenously, 78.4 percent, 81.6 percent, and 73.7 percent conceptions, respectively.⁶² Another study reported 68 percent recoveries from cystic ovaries in Guernseys and 78 percent recoveries in Holsteins by the administration of 5000 I.U. chorionic gonadotropin intravenously.⁹ Due to the cost of the product it is more economical to treat most cows with 2500 to 5000 I.U. of chorionic gonadotropin intravenously than the 10,000 I.U. dose intravenously or intramuscularly. Intramuscular injections of 1000 to 5000 units of chorionic gonadotropin in 14 cows resulted in a slightly lower conception rate of 64.3 percent.⁶² No difference was observed from year to year in the efficacy of the pituitary or chorionic gonadotropin products rich in L.H. A comparative study reported on the treatment of 278 cows with cystic ovaries with the intravenous injection of 10 RU "Vetrophin," a sheep pituitary gonadotropin, 65 cows with 5 R.U. "Vetrophin" intravenously, and 38 cows with 5000 and 10,000 IU HCG intramuscularly. Recovery and conceptions after one treatment were 65.5, 69, 78, and 71 percent, respectively, for these treatments. Thus large doses of HCG improved results only slightly.

Only one case of anaphylaxis has been observed by the author. A moderately-affected case, occurred after the administration of 5000 I.U. of human chorionic gonadotropin intravenously. No reaction has been observed or reported with the use of the sheep pituitary product, "Vetrophin."

Of 185 cows in which cysts were removed by manual pressure through the rectum at the time of treatment with either pituitary LH, or chorionic gonadotropin, 156, or 84.3 percent, recovered; 29 or 15.7 percent, did not recover. 133, or 71.9 percent, conceived; 20 or 10.8 percent, were retreated; and 32 or 17.3 percent, were sold. Of 103 cases in which the cysts were not ruptured at the time of treatment with LH, 87, or 84.5 percent, recovered; 16, or 15.5 percent, did not recover; 79 or 76.7 percent, conceived; 11, or 10.7 percent, were retreated; and 13, or 12.6 percent, were sold. No benefit resulted from removal of cysts at the time of treatment with an L.H.-rich product.^{61,62} Since trauma to and adhesions of the ovary may be produced by manual removal of cysts this practice is unnecessary and contraindicated. After

injections of LH the cysts luteinize and developing follicles may ovulate and luteinize⁷⁹ and symptoms of nymphomania cease in 3 to 6 days in affected cows that recover. Although most of the unruptured cysts luteinize, the cystic fluid may remain until a few days before the next normal estrus when the luteal tissue and the cystic fluid recede and disappear rather rapidly. A normal estrus will occur in most cows from 15 to 30 days after treatment, with most cows exhibiting estrus 20 to 25 days after treatment.

Within the last 10 years rapid advances in the study of the peptide releasing factors from the hypothalamus has resulted in the synthesis of the decapeptide gonadotropic releasing hormone (GnRH) or luteinizing hormone releasing hormone or factor (LH-RH or LH-RF) or the commercial product "Cystorelin."* This decapeptide when injected in any manner usually intramuscularly into cattle causes a dose related increase in plasma concentrations of luteinizing hormone (LH) from the anterior pituitary gland. Although doses of GnRH in Europe are higher, 0.5 to 1.5 mg., the dose used in the U.S. is 100 ug. (50 ug/ml) in 2 ml. For long existing cases, relapses, or slightly better response on initial treatments larger doses of GnRH may be used.³⁵ This product is currently cheaper in price than 5000 to 10,000 I.U. of human chorionic gonadotropin. GnRH is non-toxic even in large doses and produces no side effects or anaphylactic reactions. Refractoriness to the GnRH does not develop in cows as occurs after repeated injections of human chorionic gonadotropin (HCG), a foreign protein.

In the normal cow the rising level of estradiol early in estrus in the absence of progesterone from the corpus luteum results in the preovulatory surge of LH in cows with a serum level of 40 to 50 ng/ml that is believed to induce proteolytic enzyme synthesis in the Graafian follicle that weakens its wall resulting in ovulation. Immediately after, or even slightly before, ovulation LH induces luteinization or a conversion of the steroidogenic activity of the granulosa and theca cells from estradiol to progesterone synthesis and within 5 to 6 days the mature corpus luteum is formed that secretes progesterone to regulate the estrous cycle and, if the fertilized ovum is present, to maintain pregnancy. Progesterone has a negative feedback on the hypothalamus and the pituitary on LH release.³⁹ Cystic ovaries in cows, as indicated earlier, are due to a failure of the normal release of LH and GnRH necessary to cause ovulation and luteinization of the ovulated follicle.

Recent reports indicated the treatment of cystic ovaries with 100 ug GnRH IM caused luteinization of the cystic structures without ovulation.^{39b} Larger doses of GnRH, 0.5 to 1.5 mg or 750 to 10,000 IU HCG given IM caused ovulation of 1 to 3 cystic or mature follicles followed by the formation of corpora lutea.^{39b,71b} About 40 percent of ova recovered from these cows, following AI within 24 hours after treatment, were fertilized. Ovulation occurred about 27 hours after treatment.^{71b} Thus GnRH and HCG may induce ovulation and CL formation besides luteinizing the cystic structures. Like HCG therapy, manual rupture of the ovarian cysts is not necessary or recommended. Within 9 to 13 days after GnRH or HCG treatment the increased amount of lutein tissue produced in the cystic structures is producing a plasma level of progesterone that is similar to that in the estrous cycle in about 80 percent of the treated cows.⁴¹ The onset of estrus after treatment may range from 9 to 30 days depending on the ovarian and endocrine status of the cow.^{10,39} In the 20 percent of cows failing to respond to treatment by the re-establishment of the estrous cycle the cause may be due to the cystic structures being unable to respond to LH release because of degeneration of the granulosa and theca interna layers.^{40,41} Other causes might include: unobserved estrus, the hypothalamus and/or pituitary may not be responsive in releasing LH due to elevated estradiol concentrations,⁴¹ or high ACTH and cortisol levels may be present that suppress estrus.^{43,69}

The success or response to treatment of cystic ovaries with GnRH is about the same as with human chorionic gonadotropin (HCG).^{10,35} In 225 dairy cows with cystic ovaries treated one to three times with 100 ug of GnRH at less than 30 to more than 90 days postpartum that clinically recovered with a normal estrous cycle was 76 percent, 78 percent and 66 percent for the three treatments, respectively. The conception rate on first service after treatment was 49 percent and 83 percent of the cows eventually became pregnant at an average interval of 87 days from treatment to conception.⁷⁸ In a controlled study 114 dairy cows with cystic ovaries were divided into four equal groups and given 0 ug, 50 ug, 100 ug and 250 ug of GnRH as an intramuscular injection.^{9a} Recovery rates based on the development of a normal estrous cycle or conception were 21 percent, 64 percent, 82 percent and 77 percent. The mean days from parturition to treatment for these four groups was 63, 111, 89, and 94 days, respectively. Most cows came into estrus 18 to 23 days after treatment with GnRH, the range of days was 8 to 35.^{10,39} Other reports on the treatment of cystic ovaries with GnRH have been cited with essentially similar responses.^{25,35} In one study there was no difference in response to 10,000 I.U. of chorionic gonadotropin (HCG)

*Abbott Laboratories, Chicago, Ill.

and 250 ug GnRH.⁶¹ However early diagnosis and treatment increased the chance of recovery as pregnancy rates within 90 days postpartum for groups treated within 59 days, 60 to 120 days, 121 to 180 days and over 180 days were 48, 39, 51 and 26 percent.⁶¹ Since the incidence of recoveries are similar for GnRH and HCG, the advantages of the former are its cheaper cost and the evidence that refractoriness on repeated doses, due to the production of antibodies against a foreign protein, does not occur. If a normal estrous cycle has not occurred within 23 days of GnRH treatment, the cow should be reexamined and possibly treated again. This may be necessary in about 20 percent of the cows.

In all carefully controlled studies on bovine cystic ovaries spontaneous recoveries are reported. These are most commonly observed early in the postpartum period. About 50 percent of cows developing cystic ovaries within 45 days postpartum recovered spontaneously before 60 days postpartum.⁵⁵ In the two studies^{9a,78} 21 and 29 percent of spontaneous recoveries occurred in cows with cystic ovaries diagnosed between less than 30 to more than 110 days postpartum. Thus early postpartum examinations⁷⁷ 15 to 45 or 60 days, together with early treatment of ovarian cysts will improve the rate of recoveries. The decision for the best time to examine cows to possibly treat by rupture of cysts formed soon after calving, or treat the cows with GnRH or HCG will vary with the prevalence of cysts in the herd and the frequency and cost of the examinations.⁷⁷

The combination of GnRH or LH (HCG) and prostaglandins recently have been shown to have certain advantages in the treatment of cystic ovaries.^{10,19,35,40} Treatment of cystic ovaries with GnRH or LH (HCG) results in about 80 percent of the cows developing luteinized cysts or CL by 9 to 13 days after the injection followed by estrus 18 to 23 days (range 9 to 35 days) after the injection. If a luteolyte dose of PGF_{2a} is given 9 to 14 days after treatment with GnRH most cows will exhibit normal estrus 3 days later or 12 days after the injection of GnRH. This treatment aids in helping to synchronize estrus and shortening the time from GnRH injection to conception by 7 to 10 days in many cows.^{10,40}

The second regimen is based on the facts that HCG or GnRH will effectively cure luteal cysts as well as follicular cysts by providing or releasing LH. From 15 to 75 percent of the cystic structures on the bovine ovary are luteal cysts as determined by palpation, abattoir studied and plasma progesterone levels.^{10,19,35,61,80} The proposed and apparently successful therapy for cows with cystic ovaries consists of injecting a luteolysing dose of prostaglandin which should involute all lutein tissue in the cystic ovarian structures, followed by a dose of GnRH or HCG 3 or 4 days after the injection of PGF_{2a}. If estrus

is observed at this time, breeding is indicated. The time to the next estrus can be shortened by a second injection of PGF_{2a} 9 to 14 days after the dose of GnRH or LH. These modifications of the usual treatment with GnRH or LH may prove valuable in the treatment of cystic ovaries in certain cows despite the increased cost. Further studies are indicated.

Many cystic ovaries in dairy cows develop between 15 and 60 days postpartum when milk production is at peak levels. Recent studies have shown that plasma and pituitary levels of LH are low at parturition and increase from 8 to 30 days later.^{60b} However the pituitary is responsive to treatment with GnRH by day 14 postpartum and the resultant LH surge will cause subsequent ovulation, corpus luteum formation and the onset of estrous cycles. Fertility increased as the number of estrous cycles prior to 60 days postpartum increased.^{60b} Although more studies are indicated reports have shown that when 204 Holstein cows were given 200 ug of GnRH intramuscularly between days 8 and 23 postpartum the incidence of follicular cysts was reduced from 15.2 to 5.7 percent.^{9b} However the interval to first insemination, interval to conception and inseminations per conception did not differ from controls also bred for the first time between 80 and 90 days postpartum. In another study 100 or 250 ug. of GnRH were given to 335 dairy cows in two herds from 13 to 15 days postpartum.^{66b} In this trial the incidence of ovarian cysts in treated and control cows was similar, about 15 to 25 percent. However in one herd given the larger dose of GnRH and insemination of cows begun at 50 days postpartum the treated cows had a shorter calving to conception interval, 81 vs 96 days, a better overall conception rate, 75 vs 56 percent and a lower number of services per conception, 1.23 vs 1.74, than the controls.

If the cow has calved 50 days or more before the treatment of cystic ovaries and if no definite pathology of the genital tract is present requiring further rest or treatment, the author and others have recommended that the cow be bred the first estrus after the injection of luteinizing hormone. No observable increase in twinning or delayed conception has been caused by this practice. The practice of breeding promptly is indicated because if cows are pregnant cystic ovaries cannot recur! If cows are allowed to have two or three estrous cycles after therapy for cysts relapses are more likely to occur at each ovulatory period. In the early treatment of certain cases some veterinarians remove cysts manually without injecting LH and if there is no response they treat with LH on a return trip. In the end this procedure may be more costly to the farmer than if the veterinarian administers LH on the initial call.

If a case of cystic ovaries fails to respond to an in-

jection of LH or GnRH and a second call is made a larger dose is indicated. The author also recommends a possible change of products from a gonadotropic hormone from pituitary LH to chorionic gonadotropin, or vice versa. In 12 cases retreated with the same product 3 to 4 weeks after the first unsuccessful treatment, 5, or 41.7 percent of the animals recovered and conceived. In 31 cases of cystic ovaries in which a different product from a different source was used for the second treatment 26, or 83.9 percent, recovered and 67.7 percent of the cows conceived.⁶² Since gonadotropic hormones are protein in nature and originate from a species of animal other than the bovine species, antibodies develop from the first injection, and neutralize some or much of the same hormone when reinjected. When repeated injections of gonadotropin were used to superovulate cows the animals rapidly developed a refractoriness or inability to respond to the hormone that persisted for months. Other more recent studies have confirmed the development of antihormones against the injected gonadotropin such as HCG and PMSG. The more refined the gonadotropin the less antigenic it was in causing antihormones.

The injection of small doses, 500 to 2000 I.U. of HCG or 0.5 to 5.0 R.U. "Vetrophin" directly into the ovarian cyst by means of a fine needle inserted through the vaginal wall or ischiorectal fossa while the other hand of the operator in the cow's rectum manipulated the cystic ovary has been reported upon.^{62,75} Although the cost of the hormones used by this technique was less, the results were about the same as other modes of administration of LH. The site of the injection by-passed the body fluids to act directly on the ovarian structures to produce luteal tissue thus avoiding possible neutralization of the LH by antihormones in repeatedly treated cows. This procedure has not proved to be popular or commonly performed.

Under the influence of estrogens, early in estrus LH is released from the pituitary gland. Since progesterone and similar products suppress the release and favor the storage of gonadotropin by the pituitary gland probably by acting upon the hypothalamus to prevent the release of GnRH, these products have received attention in the treatment of cystic ovaries.³⁶ Researchers treated 100 cows that developed cystic ovaries and remained in estrus for a few days after service with 750 to 1500 mg of Repositol progesterone intramuscularly.⁷ The nymphomaniac signs terminated in most of these cows within 36 to 72 hours and 67 of the cows conceived.

Ninety-eight cows with cystic ovaries were given 109 treatments of either 50 or 100 mg. of progesterone in oil daily subcutaneously for 14 days. The cysts were not ruptured.³⁶ Normal estrous cycles and estrus resulted in 60 percent of the cows; 48.7 percent and 52.5 percent

of the cows treated with 50 and 100 mg. of progesterone, respectively, conceived. Of 30 untreated control animals with cystic ovaries only 13.3 percent conceived. The average interval from treatment to conception was about 45 days with about 2+ services per conception. Presently progesterone therapy for the treatment of cystic ovaries is seldom used.

In a discussion of the treatment of cystic ovaries in cattle the author would be remiss if he did not again call attention of his readers to the fact that this condition is frequently due to an inherited weak hormonal constitution. The repeated successful treatment of affected cows simply increases the length of time these cows remain in the herd and increases the numbers of their daughters who also have an inherited predisposition for this disease. In many cases the veterinarian would be doing the farmer and the breed a favor by declining to treat certain cows and to recommend their slaughter. Herds with a high incidence of cystic ovaries should be bred to bulls from lines free of cystic ovaries or by bulls shown to have daughters with a very low incidence of the disease.

Failure of Ovulation or Delayed Ovulation due to a failure or delay in LH release from the anterior pituitary gland and not associated with cystic ovaries may occasionally be a cause of infertility in cows and heifers. This is probably a minor cause for infertility since only 3 out of 104 repeat-breeding cows failed to ovulate.⁷¹ Failure of ovulation occurred in only 3 percent of 247 cows examined.¹¹ This low incidence of failure of ovulation is further supported by other studies.^{6,71} Ovulation failure occurred in 13 percent of heifers on their first standing estrus and in 2 percent on their second estrus.⁵³ Thus present evidence would indicate that failure of ovulation and atresia of the follicle with an absence of cystic follicles is an uncommon cause of infertility in the cow. It appears to be more common in the ewe and mare at the beginning or transitional phase of the breeding season. In a careful study of 58 cows 69 percent had ovulated by the day after estrum and 65 percent of those bred conceived. The other 31 percent of cows had ovulated by the second day after estrum and of those that were bred only 36 percent conceived.²⁸ However in a study of 118 Friesian and 161 Afrikaner cows and heifers over a 4-year period including a total of 536 estrous periods, defective ovulations occurred in 140; 47 cases or 34 percent ended in anovulation and 93 cases or 66 percent had delayed ovulation. Forty-one of the 47 anovulatory follicles regressed, 4 became follicular cysts and 2 luteal cysts. In delayed ovulation the delay was less than 48 hours in 85 percent of the cases. In 2 cases ovulation occurred 7 and 9 days after the cessation of estrus and both cows conceived to inseminations performed the day

before ovulation.⁷⁴ These authors recommended that if the follicle had not ovulated by 24 hours after service the cow should be inseminated again. In 51 cows reinseminated 24 hours after the first insemination 32 conceived while none of the 18 cows that had failed to ovulate within 24 hours of service conceived. They reported that only one of 17 cows inseminated after ovulation conceived and only one of 36 cows conceived when the follicle was manually ruptured at the time of insemination. They indicated that the two main causes for defective ovulation were nutritional deficiencies, especially during the winter months, and an hereditary predisposition characteristic of certain infertile cow families in both dairy and beef breeds. Because some reports indicated that anovulation or delayed ovulation are rare and other reports indicated they were common, more work is necessary on the incidence and importance of defective ovulation as a cause of lowered fertility. In light of the latter study it should be noted that if cows are bred early in their estrous period, which usually lasts 18 hours, range 6 to 30 hours, ovulation, which usually occurs 8 to 16 hours after the end of estrus, may not have occurred by the end of the 24 hour period after breeding in the normal cow. Thus breeding in the second half of the estrous period is most desirable. Delayed ovulation may result in aging of the sperm and ova and also a lowered rate of fertilization and a higher embryonic death rate. (See Repeat Breeders.)

Suspected failure of ovulation, or delayed ovulation may possibly be diagnosed by the palpation of a mature follicle on the ovary more than 24 to 48 hours after the end of estrus, especially if bloody mucus is in the vagina. The use of GnRH at breeding to assure ovulation only produced a very moderate increase in conception rates. Thus the cost benefit ratio may mitigate the regular use of GnRH. However in selected or problem cows where large follicles with delayed ovulation is suspected on the basis of repeated examinations of the ovary it may be used at breeding or six hours before or after breeding.^{25a} Routine doses of GnRH in estrus synchronization also has not proven advantageous. It should be noted that HCG (LH) has proven superior to GnRH in the ovulation of the donor cow for embryo transfer. There is little evidence that failure of ovulation or delayed ovulation is often repeated at consecutive estrus. If anovulation or delayed ovulation was diagnosed, rebreeding and the injection of LH or GnRH may be indicated since these hormones hasten and promote ovulation in the cow. In these cases it might be advisable to rebreed the cow again 24 hours after the first service so fresh viable sperm cells would be available when the ovum was released. More work is needed to assess the importance of delayed ovu-

lation and failure of ovulation without cystic follicles and to improve the diagnosis and treatment of these conditions.

Infertility Associated with Multiple Ovulations in Cattle

In a study of 294 ovulations at which breeding occurred, 252 were single ovulations and 42 multiple ovulations, as determined by rectal examination. The incidence of multiple ovulations was 14.3 percent. The conception rate in single ovulations was 57.5 percent, and in multiple ovulations 28.6 percent.⁴² Of these latter conceptions represented by 12 cows only 3 resulted in twin births. In a previous study in this same herd the incidence of multiple ovulations was 13.1 percent and the incidence of twinning was 1.92 percent. (See Discussion of Twinning in Unipara in Chapter IV, and Superovulation in Chapter XX.) Multiple ovulation is probably due to the release of increased amounts of FSH. Heredity and cystic ovaries may be associated or predisposing factors. Thus multiple ovulations resulted in infertility either due to defective ova incapable of fertilization or growth or because multiple ovulation may be a manifestation of an endocrine disturbance reflected in an abnormal transport of ova or failure of the proper attachment of the embryo. When twin or multiple ovulations occur from one bovine ovary and the fertilized ova develop in the horn corresponding to that ovary, a higher rate of embryonic death results than where twin ova are released from each ovary and each embryo develops in a separate horn, bicornual twins. This low survival rate in multiple ovulations and conceptions maybe a fortunate occurrence, as the harmful effects of twinning in cattle are well known. The above study may explain the occasional cases in which although on early pregnancy examination two corpora lutea are found, and twinning is therefore suspected, only a single birth occurs.⁴² The situation as detailed above is very similar to twinning in mares in which there appears to be a "mechanism" in the uterus that eliminates one of the twin embryos. (See Twinning in the Mare.)

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FAILURE OF ESTRUM, OR ANESTRUM

Failure of estrum, or anestrus, in cattle is the principal symptom of many conditions that may affect the estrous cycle (see Physiology of Reproduction). It is the most common single cause for infertility in cattle. In many instances where owners or herdsmen are negligent in observing their cows closely, anestrus is reported to the veterinarians when actually the condition does not exist. Anestrus in cows is observed most commonly either after parturition as postpartum or preservice anestrus, or following service as postservice anestrus, when conception does not occur. In heifers it is frequently observed as a herd problem especially during periods of lowered nutritive intake. Because failure of estrum is due to multiple causes often not directly related to the endocrine system, a complete history should be obtained, a careful clinical examination of the genital tract and ovaries per rectum and vagina by a speculum should be made, and a physical examination of the cow might be necessary so that an accurate differential diagnosis is possible. If more than several animals are affected it may be a herd problem involving management and/or nutrition in which case a careful herd survey and examination of all cows and their breeding records is indicated.

Unless this is done the veterinarian has permitted the owner or farmer to make the diagnosis, and treatment will be equally unreliable and erroneous. If a hormone is injected on this empirical basis neither the farmer, the animal, or the veterinarian is likely to be benefited. Following this essential examination, the cows or heifers that fail to show estrum may be divided into two classes, cows with a functional corpus luteum, and cows without a functional corpus luteum.

Cows that are found on rectal examination to have a normal functional corpus luteum present in one of the ovaries. Since cystic corpora lutea have a normal function, these are included in this class. In this class are cows or heifers that are pregnant, those with a persistent corpus luteum due to uterine pathology and those that are ovulating and cycling regularly but are not recognized as exhibiting estrum either because it is "weak" or "silent" or because the owner has failed to observe it. Normal cows have a functional corpus luteum in their ovary 85 percent of the time.

1. Anestrus due to pregnancy—All veterinarians performing regular rectal examination on cows have had many cases in which the owner has requested treatment for a heifer or cow that fails to show estrum, only to find on examination that the animal is already pregnant. The history or the owner's records can often be very misleading. This finding has occurred even in well-man-

aged herds where accurate records are kept. This serves to emphasize the importance of a careful rectal examination, including the palpation of both uterine horns to their apices, preceding treatment of any anestrus cow. It is extremely embarrassing to remove a corpus luteum or to inject an estrogen or prostaglandin to bring a cow into estrum at the request of an owner, and have the cow abort a 40- to 120-day fetus a few days later. Usually when the veterinarian tells the owner the approximate age of the conceptus the owner can recall when or how conception occurred. Only rarely is the owner at a complete loss to know how the conception occurred. If the cow's genital tract feels normal and healthy and there is a possibility of the cow having been serviced within the last 30 days, it is advisable to examine the cow two to six weeks later to determine if conception occurred before any treatment is given. Thus some cases with so-called anestrus may be pregnant and the corpus luteum, if palpable, may be the corpus luteum of pregnancy. One of the most common causes for prolonged anestrus is pregnancy. However, some pregnant cows may exhibit occasional signs of estrum, especially the first three months of gestation.⁹⁴

In 228 lactating cows which had milk progesterone levels determined twice a week for 120 days postpartum, 34 or 15 percent of the cows were inseminated when the progesterone levels were high.⁸⁶ Of these 34 cows 20 or 59 percent were probably pregnant from a prior service. Of these 20 cows inseminated when pregnant 8 or 40 percent aborted. Therefore all inseminations after the first should only deposit semen into the cervix and not into the uterus or a trained inseminator or veterinarian should decide whether to inseminate the cow or not.⁸⁶

2. Anestrus due to a retained or persistent corpus luteum—The retained or persistent corpus luteum is invariably observed in association with some uterine pathology such as: pyometra, fetal maceration, mucometra, mummified fetus and other disease states causing endometrial damage and inability to produce prostaglandins. Retained or persistent corpora lutea rarely occur in cows in the presence of a normal nonpregnant uterus.¹⁰²⁻¹⁰⁴ There is no evidence that cystic corpora lutea tend to persist longer than normal corpora lutea. The corpus luteum of pregnancy is nearly completely involuted by 7 days postpartum and it never persists.^{62,63} The most commonly observed "retained" corpus luteum occurs following breeding and conception and then 10 to 90 days later the embryo or fetus dies, is macerated, and absorbed or expelled, and the cow previously thought to be, or even diagnosed as pregnant, comes back into estrum or is examined and found not pregnant. This condition is spoken of as early embryonic or fetal death and

may be due to infectious, hormonal, genetic, physical or traumatic causes. Luteal cysts, as described under cystic ovaries, may persist for a long period and cause anestrus by secreting progesterone resulting in plasma concentrations similar to those occurring in diestrus.

(a) **Retained or persistent corpus luteum associated with gross uterine pathology.** Retained, imbedded, or persistent corpora lutea are associated with pre-service or postservice pyometra, fetal maceration, mummified fetus and rare cases of mucometra.⁷² A few heifers have been observed that failed to show estrus and on examination had functional corpora lutea and a normal uterus. When these corpora lutea were removed the heifer came into estrus and another corpus luteum developed. (See Figure 117.) This CL also persisted for months and the heifer remained anestrus. The histopathological findings in these heifers after slaughter revealed an absence of endometrial glands and in one heifer a lack of caruncles. In heifers or cows with a uterus unicornis if the corpus luteum develops on the ovary corresponding to the missing horn, a long period of anestrus may result if there is not sufficient normal endometrium or endometrial glands in the cystic apex of the defective horn to exert a luteolytic effect on the CL on that side. (See Figure 116.) This may result in a persistent corpus luteum without a pregnancy occurring. Cases of anestrus associated with uterine pathology and

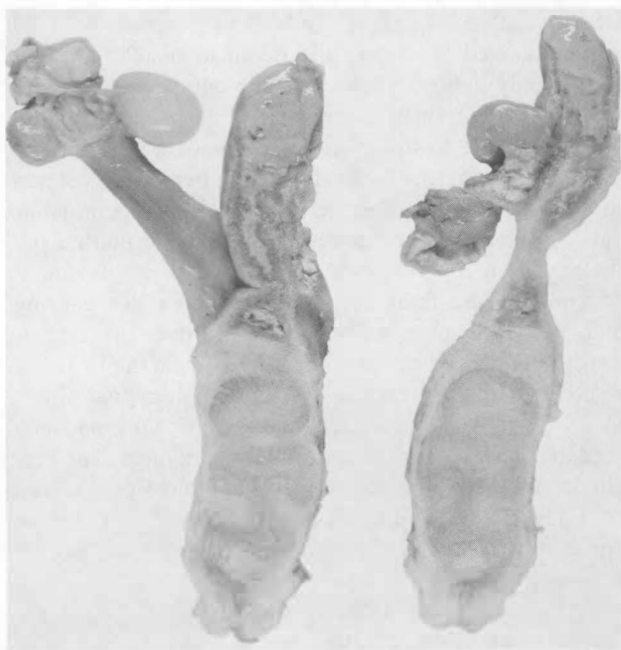


Figure 116. Anestrus Associated with Segmental Aplasia of the Bovine Uterus, Mucometra, Mucocervix and a Retained C. L.

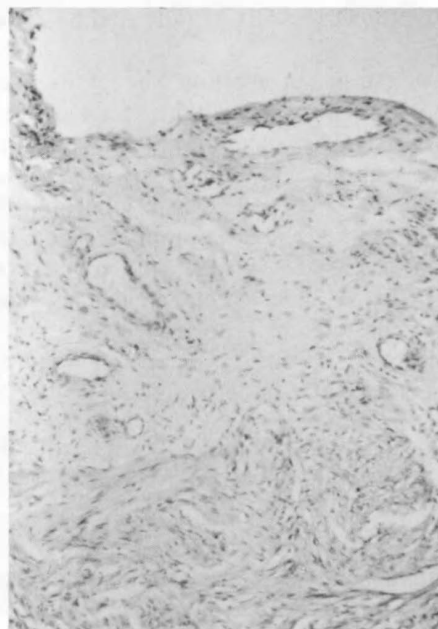


Figure 117. Congenital Absence of Endometrial Glands in a Heifer with Anestrus and a Retained C. L.

a functional corpus luteum, as well as pregnancy, are probably caused by the failure of the release of prostaglandin from the endometrium or endometrial glands.³⁶ As described previously a prolonged persistence of the CL can also be produced by hysterectomy. In these pathological cases rectal examination of the uterus will usually reveal the cause of the failure of estrus. In most of these conditions that exist for several months or more the corpus luteum becomes more centrally located in the ovary and may be more difficult to palpate. These conditions have been described already or will be described later under pathologic conditions affecting the uterus. Manual removal of the retained or imbedded corpora lutea in these cases is usually difficult and requires more pressure than do corpora lutea that have been present a shorter length of time. Injection of a luteolytic dose of prostaglandin will in most cases involute the CL, evacuate the uterus and reestablish the estrous cycle. Without a routine pregnancy examination these conditions are likely not to be diagnosed until 6 to 8 months after breeding because the cow is believed safely pregnant. In most pyometra cases secondary to retained placenta and a postpartum metritis the condition is usually characterized by a mucopurulent vaginal discharge and a failure of estrus following calving. Most cases of mucometra are characterized by chronic follicular or luteal cysts and anestrus and an absence of a normal corpus luteum. When

mucometra is associated with slight or moderate anatomic defects of the genital tract, the estrous cycle is regular and normal developing, mature, and regressing corpora lutea are present. Mucometra with a persistent corpus luteum might rarely follow early embryonic death. Occasionally these conditions may recover spontaneously but most would exist for months without estrum unless diagnosed and treated. In diagnosing and treating cases of retained corpora lutea an accurate breeding history is often helpful.

(b) **"Retained" corpus luteum associated with early embryonic or fetal death**—This condition is actually not a true "retained" corpus luteum but is a corpus luteum of a pregnancy that terminated early and was not recognized as an abortion. If because of infection or defective development, the embryo dies early, before the middle of the cycle, then estrum occurs at its usual interval; but when the embryo succumbs later, the onset of the next estrum is delayed. In many of these early embryonic deaths under 90 to 120 days, the fetus or embryo is so small it may not be seen when it is aborted, or it may remain and macerate in the uterus and further delay the onset of estrum until the trophoblast dies and is resorbed by the uterus. In this condition the so-called "retained or persistent" corpus luteum and anestrus always follow a breeding after which conception and pregnancy are not diagnosed or recognized. If early embryonic deaths are suspected as a herd or individual cow's problem, examining the uterus and ovaries and/or determining the concentration of progesterone in the milk or plasma 21 to 23 days after service may aid the diagnosis. (See Pregnancy Examinations.) The cow usually comes in estrum spontaneously after the embryo or fetus is expelled or resorbed. The condition has been commonly observed in trichomoniasis, vibriosis and trauma to the early embryo by rough manipulation of the uterus. Defective sperm or ova may result in an imperfect zygote that succumbs 15 to 90 days or more after conception and produces a similar condition of a delayed estrum following breeding. This condition of early embryonic deaths has been studied by workers associated with artificial insemination and is described under repeat breeder cows.

There is a marked difference between the percentage of cows actually pregnant and the percentage of cows apparently pregnant on nonreturns at 28 to 35 days after artificial insemination and at 60 to 90 days after insemination. This discrepancy is in part due to early death of the embryo or fetus and largely due to failure to observe estrum after an infertile service. The condition has been erroneously described clinically as "persistence or retention" of the corpus luteum.

The following comparison has been given between reported nonreturns on 4,286 cows after first insemination and actual pregnancy diagnosis by rectal examination.¹⁰

Number of Days After First Insemination	Reported Non-Return Percentages	Actual Percentage of Cows Pregnant	Percentage Difference
30-60	67.8	52.9	14.9
60-90	58.4	52.9	5.5
90-120	55.7	52.9	2.8

Thus a decline of 23.2 percent from cows supposedly pregnant at 30 to 60 days to cows actually pregnant at 90 to 120 days after the first service was reported. The figures reported may be a little higher than present figures because antibiotics were not added to the semen and vibriosis was not being controlled before 1949. On data based on about 44,000 cows in 1954 the difference between cows apparently pregnant according to 28 to 35 day nonreturns, and actual pregnancies at more than 180 days was about 16 percent and the difference between cows apparently pregnant at 60 to 90 days, as based on nonreturns, and actual pregnancies at more than 180 days was 6 percent.²⁹ By employing nonreturns to service, estrus and cyclic milk progesterone patterns, the embryonic mortality rate between 28 and 75 days after breeding was an estimated 7.2 to 12.5 percent. Failure to detect estrus following an unsuccessful insemination was the major reason for the 22.9 percent delayed returns to estrus.⁵⁰ In a study of Israeli-Friesian cattle an 8.5 percent embryonic mortality was reported between 20 and 50 days postservice.⁷⁶ Thus this postservice anestrus which occurs in 40 to 60 percent of cows in a herd¹⁰³ is comprised of both a smaller component of early embryonic death and a larger component of failure to observe subsequent estrus periods.⁹⁴ In a fertility study of nearly 10,000 Holstein cows in 125 herds in Northeastern U.S., in 1975,^{82a} the apparent incidence of unobserved postservice anestrus was greater than preservice anestrus confirming the reports by Zemjanis.¹⁰³ The average postpartum day for the first service was 87 days for 8800 cows when 60 days was the desired time. The interval from first to second service for 4300 cows was 41 days and for second the third service for 2000 cows was 40 days.

Following service many cows, 40 to 50 percent, fail to conceive; subsequently they come back in estrum after a period usually longer than the normal estrous cycle. In some instances this may be due to early embryonic death and this delayed onset of estrum or period of anestrus may be diagnosed as "persistence" or "retention" of the

corpus luteum because the cows are not known to have been pregnant, have not had a history of estrus or abortion, and have a corpus luteum on one ovary. About 18 percent of cows bred naturally or artificially returned to service within 28 days while about 25 percent returned to service after 28 days.⁸³ On careful clinical examination at weekly intervals on 426 cows in 22 herds this investigator found 332 that failed to come into estrus within 28 days of service; 234 of these were diagnosed pregnant and of those 12 aborted, 3 abortions were observed and 9 were not observed. About 48 percent of return services to artificial insemination in Kentucky occurred after a prolonged interval of 25 days or more.⁶⁷ In the experiment station herd of cattle, of 1347 cycles following service 44.8 percent were prolonged; while of 2429 cycles not following service only 26.8 percent were prolonged. Breeding cows soon after calving was not a cause for delayed returns to estrus; on the contrary there was a tendency for the cows to come back into estrus in less than 18 days when bred at 5 weeks or less after parturition.⁶⁷ The study noted that 11.5 percent of the cycle lengths were 27 to 33 days for repeat services as compared to 3.3 percent of the cycles not following service. Thus early embryonic deaths after service may be the cause of so-called "retained" corpora lutea.

(3) **Anestrus due to subestrus, "weak" or "silent" estrus**, occurs fairly often, according to many veterinarians on the basis of clinical observations. The cow may not show estrus for 30 to 120 days or longer after calving even though closely observed by a competent herdsman; but on rectal examination during this period the cow shows evidence of having ovulated by the presence of a normal corpus luteum; or occasionally the cow may be in estrus or have just ovulated, as based on the typical changes in the genital tract or ovary and by the presence of estrual mucus or metestrual bleeding.

Subestrus, weak estrus, or silent estrus, occurs more frequently between calving and 60 days than it does 60 days or more after parturition. In 286 ovulations 78 or 27.3 percent were silent.⁴⁷ The incidence of "silent" estrus during the first 60 days after calving was 44.3 percent of 140 ovulations, but only 11.0 percent of 146 ovulations were "silent" during the period of 60 to 308 days. Of cows examined that had not come into estrus within 28 days of breeding and were not pregnant, 31 or 28.2 percent exhibited "silent" estrus or subestrus.⁸³ Ovulation in all cows occurred at an average of 25.4 days earlier than the first postpartum estrus and 68 percent of the cows showed at least one "quiet" ovulation or "silent" estrus before the first clinically apparent estrus.²² Older cows, over 5 years of age, tended to show longer intervals between parturition and estrus than did

the younger cows. A high incidence of "silent" estrous cycles, when behavioral signs of standing estrus were not observed, were reported during the postpartum period in the cow.^{56,62,63} Seventy-seven percent of the cows at the first estrus after parturition, 55 percent at the second estrus, and 35 percent at the third estrus exhibited "silent" estrus. By 90 days after parturition over 93 percent of the cows had shown visible signs of estrus. Seventy-four percent of 53 heifers that reached puberty exhibited "silent" estrus at the time of their first ovulation, 43 percent at the time of the second estrus or ovulation and 21 percent at the time of the third estrus.⁶⁰ About 10 percent of the ovulations during the service period were "silent."^{90,91} These periods were observed in 16.5 percent of the cows. From these reports it is evident that "silent" estrus is probably a common cause of anestrus and loss of time in rebreeding animals. This condition is clinically characterized by failure of estrus. These animals when turned out twice a day and closely observed for 20 to 30 minutes and teased by a bull will fail to show standing estrus even though they are ovulating. In some cases occasional, mild signs of estrus might be shown. Of 20 cows bred artificially during "silent" estrus 65 percent conceived.⁹¹ The time of insemination was based on repeated rectal examinations of the ovaries and palpation of the maturing follicle. Recent studies have shown that these former reports may be incorrect if cows are observed continuously 24 hours a day or by closed circuit television.^{48,94} In this latter study although the time of first, second and third ovulations after calving were similar to the above or 19.5, 44.4 and 63.7 days, respectively, an observed estrus was detected in 50 percent, 94 percent and 100 percent of the respective three ovulations. Thus "silent" estrus, a term used by the former authors, possibly should have been "unobserved or undetected" estrus. The former is more acceptable to the herdsman! More postpartum silent estrous periods occurred in nursed cows than in cows milked twice a day. The interval from calving to first estrus was 30 days longer in nursed cows than in milked cows; the interval from the formation of the first CL to the first estrus was 30 days in nursed cows and 17 days in milked cows. The interval from calving to the first CL was 53 days in nursed cows and 36 days in milked cows.⁹⁷

The physiologic basis for the failure of typical symptoms of estrus to accompany ovulation is not known but a lack of sufficient secretion of estradiol by the mature and secondary follicles or due to a need for a higher threshold of estrogen in the central nervous system of certain individuals at certain times to produce the nervous symptoms characteristic of estrus and acceptance of the bull is questionable since all ovulating cows have

an increased concentration of estradiol in their plasma during estrus. Progesterone can potentiate the action of estrogens in bringing a cow into estrus.⁷⁷ Standing estrus may require a regressing CL still producing some progesterone to result in good signs of estrus. A recent study showed hormone levels in plasma at the onset of estrus had no effect on intensity of estrus or on conception rate. Estrous activity was greater in the morning than in the evening, in the winter than in the summer and in barn-housed cattle than those in free-stalls or on pasture. Conception rates were similar in cows bred at the time estrus detection and 12 hours later.^{25b} Certain breeds of cattle have a hereditary predisposition for "weak" estrus whereas other breeds exhibit more marked estrous symptoms.⁵² In this country the author has observed that the Guernsey and Holstein breeds are more apt to have a predisposition toward "weak" heats than is the Jersey breed.¹⁹ Certain sire lines in a herd of Holstein cows exhibited a significantly higher incidence of silent heats or quiet ovulations than others indicating that a genetic variation affects this condition.⁵¹ Cows in advanced age, arthritic cows, cows with footrot, untrimmed feet or other painful diseases may not show good signs of estrus. They may refuse to mount, or to stand to be mounted, and separate themselves from the rest of the herd. Cows on slippery concrete floors, especially during the winter months, may not exhibit signs of estrus by standing to be mounted or by mounting. Placing cows in a dirt-floored lot or area greatly facilitates estrus detection.

(4) **Anestrus due to unobserved estrus** is, on clinical examination impossible to differentiate from "silent" estrus, subestrus, or "weak" estrus. Estrous periods are usually about 18 hours in length but in some cattle, especially heifers, estrus may be only 8 to 12 hours long. In tropical countries and the southern states the length of the heat periods in the English and dairy breeds is shortened to 12 to 13 hours and in Zebu cattle estrus lasts only 5 to 8 hours. A study of Canadian cows by continuous monitoring with a television camera showed the duration of "standing" estrus to be 7.5 to 10.1 hours depending on the number of cows in estrus at the same time. About 70 percent of cows exhibited signs of estrus from 6 PM to 6 AM or during the night hours.⁴⁸ Since most cows are observed in estrus several or more hours after the onset of estrus and since the highest conception rate occurs near the middle or toward the end of estrus, it is recommended to breed cows soon after they are observed in estrus rather than 12 to 24 hours later. If a cow is still in estrus 12 hours after service she should be rebred.²⁸ During the middle of the day, especially in hot climates or when cows are eating are poor times to observe cows for estrus. When environmental temperatures

were maintained at 75 to 95° F it was shown that the duration of the estrous period was 11 hours compared to 20 hours in heifers maintained at atmospheric temperatures of 62 to 65° F.^{34,89} Under the former stress condition the intensity of estrous signs were also reduced so that the incidence of anestrus was 30 percent when signs of estrus were watched for twice a day. In the other groups without heat stress the incidence of anestrus was only 7 to 8 percent (See Bovine Reproductive Physiology). These short periods could be missed especially if the animals were turned out of the stanchions or watched only once a day. This problem and "weak" estrus are difficulties which must be overcome in educating farmers to artificial insemination. If an owner or herdsman does not watch his cows carefully at least 20 to 30 minutes 2 to 4 times a day in a yard where the cows are free to move about, many heat periods will not be observed. In the northern latitudes artificial lighting early in the morning and late at night is necessary to adequately observe cows for estrus. Cows exhibiting "weak" estrus or subestrus are fertile but often because of poor timing of the insemination, conception rates are lower. The owner or herdsman should be acquainted with the estrous symptoms of each cow, so that if certain cows show mild or slight symptoms these can be watched for and recognized. In general the larger the herd or the greater the number of cows per man, the greater the incidence of anestrus. Due to laziness, ignorance, neglect, carelessness or inability to set priorities, some farmers cannot use artificial insemination service because they fail to observe and detect estrus in many of their cows. After trying artificial insemination these farmers usually resort to the earlier method of allowing a bull to run with the herd.

Anestrus due to unobserved estrus was reported in 39 percent of 5848 reproductive cycles in dairy cows, 11 percent were in preservice cycles and 28 percent were in postservice cycles.^{101,104} These cases were called functional anestrus and 90 percent of all anestrus cycles were in this category. Only 10 percent of the anestrus cycles were due to pathological or organic causes. Twenty percent of postservice anestrus cows were not pregnant even though the herdsman assumed them to be pregnant. The economic importance and monetary loss due to unobserved estrus was calculated to be 30 and 42 production days for preservice and postservice anestrus, respectively. If this loss was valued at \$.50 or \$1.00 per day, the annual loss for each dairy herd for the 13 dairies comprising the 2600 cattle in the study was \$750 or \$1500, respectively.

Herds in which continuous observation, 24 hours a day, was maintained 90 to 95 percent of the cows were observed in estrus within a 24 day period.^{48,94} Only 4 to

10 percent of the cows were anestrous without detectable abnormalities. In the average fairly well-managed herd only 40 to 60 percent of the estrous periods are noted. With the advent of larger herds and fewer caretakers per herd the incidence of anestrous due to unobserved estrus continues to rise and has become the greatest single cause for infertility in large dairy herds being bred artificially.

The prognosis in cases of failure of estrus or anestrum cows found to have a normal functional corpus luteum on repeated rectal examinations depends upon the cause. In anestrum due to a persistent corpus luteum caused by some uterine pathology the prognosis is good in fetal mummification and early embryonic deaths. While in pyometra the prognosis is fair to good and in late fetal maceration, mucometra or a congenital absence of uterine glands in the endometrium the prognosis is guarded to poor. The longer the condition, such as pyometra, has existed the poorer the prognosis for the future breeding life of the cow. Conception following early embryonic deaths may be delayed, especially in diseases such as vibriosis. In "weak," "silent" or unobserved estrus the prognosis is usually fair to good as close observation reduces the incidence of anestrum due to this cause.

Treatment of failure of estrus or anestrum in cows should be based on a careful differential diagnosis, often requiring careful recordings of repeated rectal examinations.

The treatment of retained or persistent corpora lutea due to uterine pathology such as pyometra, mucometra, mummified or macerated fetuses will be described later in this text. These conditions often respond to the injection of 40 to 100 mg of stilbestrol or 4 to 10 mg of estradiol, repeated in 2 to 4 days if necessary for several injections or prostaglandins to cause an involution of the retained corpus luteum, the evacuation of the uterus, and the reestablishment of the estrous cycle. In a few cases manual removal of the corpus luteum, as described below, may be indicated but the dangers associated with this treatment, especially in pyometra, greatly limit this mode of therapy. The use of prostaglandin F_{2a} (Lutalyse), 20 to 35 mg, or cloprostenol (Estrumate), a prostaglandin analogue, 250 to 500 μ g, intramuscularly are preferred treatments over estradiol preparations such as estradiol cypionate, and possibly estradiol valerate, to cause luteolysis of the corpus luteum, evacuation of the uterus and produce normal estrous cycles. Luteal cysts causing anestrum and elevated progesterone levels in blood plasma may be treated with GnRH, HCG or prostaglandins as described under cystic ovaries, usually with excellent results.

Treatment of persistence of the corpus luteum due to long-standing pyometra and fetal maceration with the

presence of bones in the uterus may occasionally result in the restoration of the estrous cycle but conception usually fails to occur due to the chronic uterine damage caused by the infectious process. In some instances a laparohysterotomy may be necessary to remove the bones from the uterus. In the rare cases of heifers with a congenital lack of endometrial glands causing the persistence of the corpus luteum, no treatment is possible. It might be desirable to take an endometrial biopsy or recover the uterus at slaughter so the diagnosis may be confirmed by histopathological methods.

Treatment of anestrum due to early embryonic death is usually not necessary since the embryo or fetus and its membranes are expelled, or macerated and resorbed. The corpus luteum of that pregnancy involutes and estrous cycles are reestablished. If the latter course is followed it may require two to six weeks following the death of the zygote before estrus occurs. Detection of anestrum due to early or late embryonic deaths, and post-service anestrum due to "silent," "weak" or unobserved estrus requires an early accurate pregnancy diagnosis between 35 to 45 days of pregnancy and possibly a second examination in certain cows or herds with vibriosis, trichomoniasis or a high incidence of fetal mummification at 80 to 150 days or more days of gestation. As previously mentioned, examination of the genital tract and ovaries for the presence of a corpus luteum and a lack of estrus or high progesterone levels 21 to 23 days after service can provide an early presumptive diagnosis of pregnancy and an early indication of embryonic death. Because anestrum of pregnancy is expected after service many owners fail to realize the importance of early pregnancy diagnosis to reduce the serious losses incurred due to post-service anestrum in cows failing to conceive or affected with early embryonic deaths.^{102,104}

Treatment of failure of estrus or anestrum, in the common instances of "weak" or subestrum, "silent" estrus or unobserved estrus, often requires careful, accurately recorded examinations of the genital tract of affected cows, careful assessment of herd management practices, and diplomatic education and instructions for the herdsman and cattlemen. Cows or heifers with a preservice or postparturient anestrum should be examined at 50 to 60 days postpartum or at 15 to 18 months of age, respectively, if they have not exhibited estrus by that time. A variety of treatment regimens, some already suggested under the prior discussion of the etiology of anestrum, have been used. These include:

(a) Improved management practices—Owners and herdsman often need to be trained in how to observe cows for estrus. If services per conception are low (1.2) and the average number of days open are high (150) on

a herd basis, estrus detection would only be 25 percent. While another herd with 2.5 services per conception, 115 days open would have an excellent estrus detection rate of 80 percent and etc.^{9b} The signs and degrees of external manifestations of proestrus, estrus and postestrus should be thoroughly understood.^{3a,94} Cows to be observed for estrus should be grouped or turned out together and watched carefully for 20 to 60 or more minutes twice or more times per day especially during periods of activity such as before and after milking and during the early morning, evening and night hours. Observing cows during the feeding period is not satisfactory. Observing cows on pasture is better than in barnyards.⁹⁴

Signs of estrus in order of their importance or significance include:⁹⁴

- (a) Standing immobile to be mounted—This is the most important single sign and observed in 79 percent of cows in estrus. Standing heat was observed in 4.5 percent of cows not in estrus and in 7.3 percent of standing heats were seen in pregnant cows.
- (b) Mounting other cows repeatedly, exhibiting both homosexual and heterosexual activity.
- (c) Ruffled, scraped or rubbed rump and tailhead. These signs are misleading as they persist for 4 to 6 days.
- (d) Group activity of sexually active cows is important especially at night. It includes cows in estrus or proestrus and nymphomaniacs. These cows often stand close together within a few feet of each other. Moving animals and driving helps the owner observe signs of estrus. Don't isolate cows in estrus from a herd as they are excellent heat detectors.
- (e) Restlessness—if on pasture cows interrupt grazing and roam around, increased activity, can use pedometers on legs but they are often lost.⁹³ If tied, cows often remain standing rather than lie down. By using pedometers it was determined that cows in free stalls and in comfort stalls were 4 and 2.75 times respectively more active during estrus than when not in estrus.^{47b}
- (f) Vulva swollen, edematous, relaxed—This is seen in only a few cows and is unreliable.
- (g) Stringy mucus hanging from vulva especially after mounting or lying down. This useful but seen infrequently.
- (h) Sniffing and licking of vulva, flehmen reaction, also chin resting and rubbing cow on rump.
- (i) Tail raising and switching, frequent urination and bellowing is also seen in cows in diestrus.

Thus these are all signs of estrus but each alone, except possibly (a) are not highly dependable.^{3a,94} Each farm must select procedures and the men to observe, record

and get cows bred early in the postpartum period so calving intervals of 12 to 13 months are realized. Competent, accurate recognition of all or a high percentage of estrous periods in cows from the time of first desired breeding until after they are diagnosed pregnant is essential to a satisfactory herd reproductive program. Careful records of these observations on properly and easily identified cows should be made before, during and after the breeding period. The use of heat expectancy charts are very helpful if records of previous estrous periods are accurately recorded. The use of teaser or "gomer" animals will be discussed. Some owners are incapable of properly observing cows for estrus or unwilling to spend the time to do so properly. In this instance breeding bull(s) should be run with the herd as an economically viable artificial insemination program is impossible to accomplish. In stanchion barns it is desirable to turn cows out of the barn twice or three times a day even in the winter months and observe the cows carefully. In a stanchion barn the tails and buttocks of the cows should be carefully observed daily to detect bleeding or a clear mucous discharge. In a dark barn a flashlight might prove helpful in this examination. As an aid in stimulating closer observation of cows for estrus some owners offer incentive payments to hired men or herdsman detecting cows in estrus and conceiving to a service at that estrus. The economic importance of a conscientious, observant herdsman or owner cannot be overestimated in maintaining a good conception rate and a short interval between calvings in a herd.

Heat Detection Aids or Treatment for Anestrus that may be used to supplement, not replace, careful, frequent visual observation of the herd include many techniques or practices.

(a) Cattlemen have used a cheap, plastic heat detecting device* that is glued to the top of the sacrum of postpartum cows due to be bred and of cows after breeding to assist in detecting estrous periods. When a cow in estrus is mounted by another cow or teaser bull the normally white plastic device turns red due to the release of a dye due to pressure on the device by the brisket of the mounting animal.¹⁷ These detectors may be helpful to farmers or ranchers with cattle on pasture. Cows should be examined twice a day. If a detector is only partially red that cow is often not in estrus. An Australian study on pastured cattle indicated that Kamar detectors were 90 percent effective in detecting estrus vs. 56 percent by observation alone. One drawback was that about 25 percent of them may be lost or rubbed off by mounting.

*Heat-mount Detectors by Kamar Inc., Earl D. Smith, Box 26, Steamboat Springs, Colo., 80447.

These cows were usually in estrus. Some farmers use a colored tape around the tail as well as a Kamar detector.⁹⁴ Other farmers will use a colored marking chalk or a water-soluble latex paste on the tailhead as an aid to detect estrus. Another alternative to a Kamar detector or chalk applied to the tailhead is to apply a green water-soluble plastic paint with a roller from the first sacral to the fourth coccygeal vertebrae from calving to confirmed pregnancy. In one large herd this aid increased the detection of estrus before postpartum day 60 from about 62 to 95 percent.^{94b} Conversely a study in Northeastern U.S. indicated that visual observation was 93 to 97 percent accurate in detecting estrus in dairy cows compared with the 82 to 88 percent accuracy of Kamar heat detectors.⁷⁰

(b) Teaser or "gomer" bulls, nymphomaniac cows, or cull or ovariectomized cows injected with repeated, large doses of testosterone have been used to aid in detecting cows in estrus. If bulls are only vasectomized they may spread venereal diseases in the herd. Also such teaser bulls are seldom kept beyond one year and must be replaced and there are problems when bulls are allowed to run with the herd.⁹⁴

In large, artificially-inseminated dairy or beef herds in which the detection of cows in estrus is difficult, one or more vasectomized young bulls may be allowed to run with the herd. These bulls, if used properly, are very efficient in detecting cows in estrus. Young disease-free bulls can be vasectomized in the standing position under epidural and local anesthesia or they may be cast, tied, and rolled on their backs and vasectomized under local anesthesia. Using careful clean surgical technique the operator makes separate incisions through the skin and the tunics investing each spermatic cord. The hard cord-like vas deferens is separated from the plexus of coiled veins and arteries. Two ligatures are placed on each vas about 2 inches apart and 1 inch of the vas is removed. The skin incisions are closed and antibiotics are administered for 4 to 5 days. Semen should be collected once a week for 3 weeks. By this time practically no spermatozoa are in the ejaculate and those that are present are dead.

Several cases have been reported where apparently properly vasectomized bulls regained their ability to fertilize cows. In humans sperm granulomas following vasectomy were common and 5 of 432 vasectomy cases recanalized.⁷³ The cut ends of the vas deferens should be fulgurized by electrocautery and the sheath of the vas deferens should be ligated or closed over the cut end of the distal portion of the vas to prevent spontaneous recanalization. It might also be advisable for the operator to place the removed sections of the vasa deferentia into

a 10 percent formalin solution and send them to a laboratory for histological confirmation of the removed tissue to prevent possible errors and lawsuits.

Other methods of preparing teaser or "gomer" bulls have been described. Epididymectomy by incising the bottom of the scrotum separating the tail of the epididymis from the testis, ligating the body of the epididymis and the vas deferens with nylon and removing the tail of the epididymis was recommended.^{65,95} This technique is probably better than the injection of a sclerosing agent into the tail of the epididymis,¹⁴ or the crushing of the tail of the epididymis with a Burdizzo emasculatome. These above methods do not prevent normal intromission and the possible spread of venereal diseases such as vibriosis and trichomoniasis. However teaser bulls prepared by the above methods retain a stronger sexual desire and drive than teaser bulls prepared by various operations on the penis and sheath that prevent normal intromission.

Operations on the penis and sheath to prevent conception include: (1) cutting the penis midway between the anus and scrotum and suturing it to the skin;⁸⁴ (2) placing three or four stainless steel or nylon sutures into the dorsal part of the penis cranial to the scrotum and suturing the penis to the abdominal wall;^{33,80} (3) making a small ventral incision in the skin and prepuce two to three inches behind the preputial office, suturing the skin and preputial membrane and inserting a 3/8 inch plastic urine drain for five days, followed by the dissecting apart of the skin and preputial membrane at the preputial orifice and suturing the inside membrane and outside skin to make a blind pouch to contain the penis;⁸⁰ (4) and incising of the skin around the preputial orifice and suturing the orifice so it is directed laterally instead of cranially, so the penis on erection is also protruded laterally. These operations and their modifications should be performed under good anesthesia and in an aseptic manner for best results. A male pseudohermaphrodite, a nymphomaniac cow or a cow or steer treated repeatedly with testosterone⁴⁹ may also be used as a teaser animal if it has sufficient sex drive. These latter animals have not been highly successful as estrus detectors.³⁰ (See Chap. XIX, Artificial Insemination.)

Bulls selected as "teaser" or "gomer" animals should have a strong, vigorous sex drive. If possible it may be desirable to turn these bulls out with the herd only for short periods in the morning and evening and then to alternate bulls to maintain their sex drive. A New Zealand company* has marketed a marking device for bulls

*Chin-Ball Mating Device, Frank Paviour Ltd., Mahana Rd. TeRapa, Hamilton New Zealand.

consisting of a small square stainless steel unit containing an exposed freely rotating steel ball that is fastened securely under the jaw by a special halter. The marker material comes in a variety of colors and is placed in the steel unit where it will store indefinitely. When the bull mounts a cow the marking material is rubbed in streaks down her back. These marks will last for 2 weeks but can be washed off with a detergent. One filling of the steel container is sufficient to mark 75 to 80 cows. These chin-ball markers must be kept filled with ink to be effective. Occasionally a bull on pasture with a herd will select a "harem" of cows and ignore the other cows. It was reported that smearing the brisket and inside of the legs with titanium oxide and grease was more effective than the chin-ball marker.⁹⁴ Some ranchers will have a bull in a pen near water, in a corral near salt or feed, or run their cows across a fence from yearling bulls. In these instances cows in estrus will gravitate toward the male animals and be easier to pick up.

(c) Drawing a milk sample from cows at the time of breeding and submitting it, with others, to a laboratory for **progesterone assay** is a simple and highly effective practice to determine the efficiency of a herdsman in detecting cows in estrus. It is also helpful in problem cows, if samples are taken 2 or 3 times a week for 3 weeks, to tell when the cow is in estrus or whether she is cycling. Milk samples taken at insemination and 21 to 24 days later from over 400 dairy cows in Northeastern U.S. showed that only 5.5 percent were inseminated at the wrong time, that is, when progesterone levels were elevated.⁷⁰ High progesterone levels were found in only 2.9 percent of cows in standing estrus, 2.6 percent riding other cows, 3.6 percent with roughened tailhead and 4.5 to 7.1 percent of cows that were unusually active, bawling or with clear or bloody mucus on the vulva. The Kamar heat detectors were not as accurate as visual observation. High progesterone levels at insemination were recorded in 12.4 percent of cows with full red Kamars and 18.3 percent with part red Kamars.⁷⁰ Besides the above uses for progesterone determination on milk, it will help monitor possible embryonic deaths, determine nonpregnant cows with good accuracy (90+ percent) but not pregnant cows (80 percent) 21 to 23 days after service.³² This test for progesterone because of time required for laboratory testing is not satisfactory for determining the time of insemination.

(d) The **electronic probe measurements** of electrical resistance of vaginal mucus reveals low resistance at estrus and correlated well with low milk progesterone concentrations, visual observations of estrus and positive Kamar heat detectors.^{32,42} This improved probe is inserted into the vagina every second or third day and re-

sistance readings of the dorsal and ventral vaginal mucus are recorded. The instrument is cleaned and disinfected between cows and cows must be confined for examination. Conception rates after insemination were similar where estrus was detected by visual examination and where estrus was detected by the probe when the cows were not seen in estrus.

(e) Other tests on bovine cervical mucus such as crystallization pattern or "ferming," glucose content, viscosity and pH either require laboratory tests, are laborious or not practical.^{30,94} Temperature monitoring to detect estrus is not yet practical.⁷⁴ In the cow body temperatures tend to decline slightly but noticeable with the involution of the corpora luteum and increase slightly during estrus because of increased activity. Good breeding records, the careful maintenance of a heat expectancy chart for each cow, and frequent examination of "problem" cows by a veterinarian who can predict the approximate time estrus are practices to follow in many "anestrous" cycling cows and can be helpful in controlling this common infertility problem. Rectal palpation of the genital tract and ovaries of a number of anestrous cows in a herd can readily diagnose "inactive" or non-functional ovaries without corpora lutea due to a low plane of nutrition, debility, a negative energy balance, failure to achieve puberty or a lack of estrous cycling.

(f) Frequent rectal, and if necessary vaginal, examinations of the genital tract by a veterinarian will determine the proper time to inseminate cycling cows with "weak," "silent" or unobserved estrus. The technique for predicting the time of estrus which is based on the physiologic and anatomical changes occurring in the genital tract of the cow during the estrous cycles have been described.^{46,59,85,102,104}

During proestrus, days 17 to 20 of the cycle, follicular growth is occurring and culminates in the mature Graafian follicle.⁶⁹ The corpus luteum is regressing in size, protrudes less above the surface of the ovary and becomes more firm in consistency. The uterus is developing increased tonus. On vaginal examination the last two days of proestrus the vaginal and cervical mucosa are becoming more pink, congested and edematous. The cervix becomes more relaxed and initially a cloudy and then a clear stringy mucus characteristic of estrus comes from it and collects in the anterior vagina. The cow will be in estrus within 1 to 3 days.

During estrus, day 0 or 1 of the cycle, the cow is receptive to the bull, stands to be mounted, and the changes described as occurring during proestrus are more prominent. The vulva is often edematous and relaxed. The corpus luteum is small and firm and the follicle is nearly mature, 1 to 1.5 cm. in diameter. This is the most easily

diagnosed stage of the cycle. The cow should be bred. If the cow exhibits "silent" estrus rebreeding the following day may be indicated if ovulation has not occurred.

During early postestrus or metestrus, day 1 or 2, the follicle may be soft and fluctuating and easily ruptures on pressure. This should be avoided. In most cases ovulation has occurred and the site feels like a crater-like depression 1 to 1-1/2 cm. in diameter in one of the ovaries. The uterus is less tonic but more edematous and thick-walled. The corpus luteum of the previous cycle is difficult to detect. Metrorrhagia may be observed by the presence of bloody mucus at the vulvar lips, on the tail or buttocks or by vaginal examination. This discharge may also be observed through day 3 of the cycle. A few atretic follicles may be present.

During late postestrus or metestrus, days 3 to 6 of the cycle the soft small, developing corpus luteum may be palpated and is growing rapidly, 1-1/2 to 2+ cm. in diameter, and is fairly soft in consistency. The uterus decreasingly lacks tone and loses its edema.

During diestrus, days 7 through 16 or 17, the longest stage of the cycle, the corpus luteum is mature, large and liver-like in consistency. The uterus is quiescent but not atonic. During this period some growth of small follicles occurs and results in one or more palpable follicles at 10 to 12 days that become atretic and regress by the end of this period. During this period the vaginal and cervical mucosa is rather pale and dry. The mucus is usually scant and sticky.

With practice a veterinarian can develop his skills to predict the occurrence of estrus with a high degree of accuracy. The efficacy of this method was excellent. Repeated examinations at 2 to 3 day intervals may be necessary. Sixty-nine percent of the cows examined showed estrus within 23 days.¹⁰⁴ The rate of conception on the first estrus was 10 percent better than that following removal of the corpus luteum, 55.7 percent vs 45.7 percent, respectively. Because of the dangers associated with enucleation of the corpus luteum, estrus prediction and prostaglandin injection are the methods of choice for handling anestrus due to "weak," "silent," or unobserved estrus in cycling cows. Thus rectal palpation can readily determine if the cow is cycling, and the approximate stage of the cycle. Laparoscopic examination of the bovine ovaries has been described.

(g) The removal of the corpus luteum by manual pressure through the rectal wall was formerly, 1920 through 1960, frequently employed in the treatment of anestrus in cattle when a functional corpus luteum was present. This method consists of grasping the ovary in a fold of the rectal wall between the fingers and first knuckle of

the thumb and pressing over the proximal end of the corpus luteum and enucleating it from the ovary. Care should be used so as not to rupture the rectal wall. The best time to remove the corpus luteum was during the middle of diestrus.³ Earlier removal of the soft C.L. may result in incomplete removal, and in proestrus the difficulty of removal increases. Some advocate squeezing through the tougher vaginal wall but this is usually not necessary since most corpora lutea are not centrally located and covered by a heavy capsule as occurs in long-standing retained corpora lutea.

Although removal of the corpus luteum formerly was a common form of therapy it should seldom be used and then probably as a last resort because of the possible dangers from its practice. Manual removal of the corpus luteum in cows with pyometra or other uterine infections is dangerous due to adhesions and ovaritis that may follow. In a removal of the corpus luteum the cow should not be pregnant or abortion will usually occur. After the corpus luteum is removed it should be dropped into the abdominal cavity and not into the ovarian bursa, where it may cause extensive adhesions. Adhesions of the ovary and, especially the fimbriated portion of the oviduct on the medial free border of the ovarian ventricle frequently follow rough manipulations even though bleeding may not be severe. Ovarian adhesions due to rough manipulation of the ovary was a common cause of permanent sterility.^{25,57,58} After removal of the corpus luteum excessive bleeding may take place from the ovary and cause a large hematoma around the ovary, permanent adhesions, and sterility. Fatal bleeding from the site of an enucleated corpus luteum has occasionally been reported. The incidence of fatal hemorrhage has been reported to be 1:1000 to 1:9000 removals of the corpus luteum.⁸⁷ The author has not been so fortunate as in his experience fatalities occurred at a rate of 1 to 300 to 500 enucleations. The method of expression of the corpus luteum had no influence on the fatalities. Removal of the corpus luteum can result in a loss of as much as 7 liters of blood into the peritoneal cavity.^{58,59} The removal of an embedded corpus luteum resulted in a loss of one liter of blood. In 22 to 25 cases in which the corpus luteum of the estrous cycle was removed, bleeding of one to three liters of blood was reported. In some cases the cow will temporarily develop a rapid pulse, tympany, and anorexia after removal of a corpus luteum. The manual ovarian treatment for anestrus was discontinued in experiments because the percent of conceptions showed no improvement over the controls, and furthermore removal of the corpus luteum produced permanent damage in a number of cases. Manual compression of the ovary for at least 5 minutes after removal of a corpus

luteum was recommended as a means of controlling bleeding. It is doubtful that epinephrine or other drugs administered parenterally will effectively prevent bleeding and the former drug may even be contraindicated. Many workers have reported that removal of the corpus luteum seldom results in any permanent trauma or adhesions; their observations were, however, only clinical. Because of these observations the author does not recommend removal of the corpus luteum in cows except in rare selected cases or only as a last resort. Properly used estrogen or preferably prostaglandin therapy will result in the involution of the corpus luteum without the dangers present in manual removal. Enucleation of the corpus luteum was followed by the same pattern of hormone secretion as that following the administration of a luteolytic dose of various prostaglandins, namely a sharp decline in plasma progesterone levels and a rise in LH levels.^{72a} Because manual removal of the corpus luteum is possible only in the cow of our domestic animals, this is not a sufficient reason to employ this mode of treatment in the bovine species. In cows of lesser value or in cows in which the production of milk is more important than the value of their offspring, the amount of damage or risk may not be great enough to prohibit the enucleation procedure.

The following reports from the literature summarize the results of manual removal of the corpus luteum. (See Table 19). From this table it appears that removal of the corpus luteum usually results in observable estrum in about 50 to 80 percent of the cases within 2 to 7 days, with conceptions in 25 to 70 percent of those cows bred on

the induced first estrum. In the author's experience removal of the corpus luteum from normal cows will result in about 50 percent conceptions at the next service a few days later. Most cows show estrum the third or fourth day after removal of the corpus luteum. A number of workers reported that the induced estrum frequently was "silent," or unobserved, and the animal should be watched closely for signs of estrum. Possibly this condition of "silent" estrum was the reason for the diagnosis and removal of the "retained" corpus luteum. If estrum is not observed the cow may be bred three to four days after the manual removal of the corpus luteum if conception is desired. If the cow shows estrum on the fifth day she should be rebred. Nearly 50 percent of normal cows thus treated will conceive. If the cow has a normal genital tract and is in anestrus due to "silent," or unobserved heat, removal of the corpus luteum should result in a higher rate of conception on the first estrum than if the retained corpus luteum was due to an embryonic death caused by vibriosis or some other infection in which a mild endometritis may be present. These same factors would also influence the conception rate obtained after the use of hormones.

(h) Hormonal therapy for anestrus—Estrogens have been shown to cause regression of the corpus luteum.^{20,29} The effect of estrogens on the corpus luteum is not so marked in hysterectomized heifers as in intact heifers so there is probably an interreaction with the luteolytic mechanisms in the endometrium or endometrial glands. Estrogens probably induce regression by also decreasing the level of circulating LH.²⁰ Five mg. of estradiol val-

Table 19. Summary of Selected Reports of the Manual Removal of the Corpus Luteum in Nonpregnant Cows

Author	Number of cows	Cows observed in estrum		Days estrum occurred	Conceptions
		No.	Percent		
Wright ⁹⁹	51	36	70	1 to 5	18, or 50% of those in estrum
Hofstad ⁴⁴	332	203	61.1	2 to 9	59, or 29.1% of those in estrum
Stalfors ⁸¹	105			3 to 10	38, or 35.6% of the total treated
Hancock ³⁹	70	35	50	2 to 7	10, or 28.5% of those in estrum
Lindley ⁵⁵	54	27	50		13, or 24.1%
Gibbons ³⁵	155	98	64.9	1 to 15	51, or 52.1%, on first service
Teige and Jakobsen	2746		62.5	1 to 7	49.7 to 58.7%

erate given as a single dose intramuscularly on the third or fourth to eighth or ninth day of the estrous cycle caused luteal regression in 17 to 20 heifers with 15 showing estrum before day 17 of the cycle.⁹⁶ Seven of 10 heifers injected on days 15 or 16 of the cycle developed large cystic ovaries and many developed signs of nymphomania. Other forms of estrogen caused a similar regression of the corpus luteum. The author has confirmed the effects of 5 to 10 mg. of estradiol valerate in inducing regression of the corpus luteum. Estradiol cyclopentylpropionate (ECP) as a single intramuscular dose to cause luteolysis has not proven to be as effective as estradiol valerate or the prostaglandins.^{75a} He has also produced luteal regression with 40 to 100 mg. of diethylstilbestrol but this tends to require a second or third injection at 48 hour intervals. One or possibly two injections of 3 to 10 mg. of estradiol at three day intervals or estrone, 5 to 15 mg., in a similar manner also will induce luteal regression either during metestrus or diestrus or in cases of retained corpora lutea associated with pyometra, mummified fetus or mucometra. In pyometra high and prolonged doses of estrogens such as 100 mg. of repositol stilbestrol may result in abnormal motility or peristalsis of the oviduct resulting in the introduction of infectious organisms from the uterus to the area of the ovarian bursa or fimbria of the oviduct causing ovaritis and adhesions even in cases where no ovarian manipulations were made. Cystic ovaries may occasionally follow estrogenic therapy. These occur most commonly when estrogens are given in late diestrus or in proestrus. They are rare in cases of retained corpora lutea. Large doses of greater than 4 mg. of estradiol and 40 mg. of stilbestrol are more apt to result in cystic ovaries than are smaller doses of estrogens.

Most earlier studies on the use of estrogens for the treatment of anestrus were uncontrolled and empirical. Factors that were not considered in most studies were the cause for the failure of estrus or the type of anestrus; the high rate of spontaneous recoveries and conceptions in cows with normal estrous cycles and genital tracts but having "silent," "weak" or unobserved estrous periods; the time following treatment that estrus and conception occurred, and whether normal ovulation occurred at that estrus or whether the signs of estrus that immediately followed the injection were due to the estrogenic hormone. Even spayed cows will exhibit estrus after an injection of an estrogen! Estrogenic hormones do not produce ovulation except low doses in late proestrus or very early estrus that simulate the rise in blood concentrations due to production of estrogens from the Graafian follicle causing the LH surge. The use of low doses of estrogens or estrogens and progesterone a day or two before an

expected estrus to improve the external signs of estrus has not proven of value and may lower the conception rate. Although estrogens have been widely used in the past in an empirical and haphazard manner for the treatment of anestrus, reports indicate that this type of therapy is of no, or questionable, value and may actually reduce the conception rate compared to heat prediction, removal of the corpus luteum or injection of a luteolytic dose of prostaglandin.

Although **prostaglandins** either **Lutalyse** (PGF_{2a}) 20 to 30 mg., or **Estrumate**, cloprostenol (a prostaglandin analogue) 250 to 500 ug or others are commonly used to produce luteolysis or involution of a functional or mature corpus luteum from day 6 to day 16 of the estrous cycle, or a persistent C.L. associated with uterine pathology such as pyometra or mummified fetus or for a luteal cyst. The use of such products in lactating cows have now been approved in the U.S. Fortunately the prostaglandins are shortlived and are rapidly broken down so the drug or its metabolites are only present at very low levels in the milk by the second milking. An adequate dose of prostaglandin or its analogue will act rapidly in involuting the C.L., causing a rapid cessation of progesterone production. The onset of the next estrus, as with the manual removal of the corpus luteum, occurs within 3 to 5 days, range 2 to 7 days. Giving two doses of prostaglandin or its analogue 10 to 12 days apart will cause nearly all healthy, cycling cows to come into estrum within 3 to 5 days. As mentioned earlier in this Chapter treated cows may be artificially inseminated when estrum is detected or by breeding twice AI at 72 and 90 hours or once about 80 hours after the injection. (See Estrus Synchronization.) If routine rectal examinations are performed by a veterinarian in cows during the postpartum period and anestrus due to unobserved estrus in cycling cows is a problem, selected animals may be treated during diestrus. Estrus is thus synchronized so artificial insemination and early conception is possible.^{75c} (See Estrus Synchronization with Prostaglandins.) A more desirable procedure than this is to establish an effective breeding program including careful observations and properly timed breeding of cows rather than relying on hormones for the detection of estrus. Repeated treatments of prostaglandins in a cow have not been shown to be contraindicated as is manual removal of the corpus luteum. Administration of prostaglandins prior to day 6 after estrus or in cows with follicular cysts or with "inactive" ovaries due to debility will be ineffective in establishing a normal estrous cycle.

Estrus synchronization by using progesterone, progestogens, estradiol valerate, prostaglandins F_{2a}, cloprostenol (a prostaglandin analogue) or a combination of

these drugs as described earlier in this chapter may aid in the detection of estrum in a similar manner as removal of the corpus luteum. With estrous synchronization good management is still necessary to detect estrus for proper timing of artificial insemination. Conception rates immediately following estrous synchronization are usually lower than normal if progesterone or progestogens have been employed unless the hormone can be removed from the body promptly (See Estrus Synchronization).

Since so-called "anestrous" cows with normal uteri and corpora lutea on the ovaries are probably cycling regularly most or all treated or untreated cows will show an observable normal estrus within 30 days. This probably accounts for the many early reports of successful treatments for anestrus in cattle. At present it appears that most types of anestrus except possibly underfeeding and gross pathology of the uterus, cervix, or ovaries are self-limiting and that recovery is usually spontaneous. For this reason the author firmly believes that hormone treatment or removal of the corpus luteum for correction of most cases of anestrus is of secondary importance to an accurate diagnosis. During the past 25 years the author has seldom relied on endocrine therapy to relieve anestrus which is a symptom most commonly associated with unobserved estrus. Hormones are used to correct uterine pathology associated with a persistent corpus luteum and for treating luteal and follicular cysts causing anestrus.

Anestrus cows with small or inactive ovaries with no functional corpus luteum palpable per rectum. These cows together with pregnant cows and cows with retained corpora lutea associated with uterine pathology are non-cycling cows. These non-cycling dairy cows comprise about 10 percent of all anestrous cows.¹⁰⁴ In beef cattle herds on range this percentage may be larger due to nutritive deficiencies especially in postpartum heifers.

(1) Due to "silent" or subestrus, or due to unobserved estrus, cycling cows may during the period of one to two days before, during, and one to three days after estrus, have only a small corpus luteum that might lead one on a single rapid examination to a diagnosis of anestrus due to failure of ovarian activity or nonfunctional ovaries. Careful examination usually reveals the uterus to be tonic and erect, a condition not seen in true anestrus or failure of the estrous cycle. If the ovaries are examined before ovulation the mature follicle and the regressing firm C.L. may be palpated, or if soon after ovulation the site of ovulation or a slight crepitation characteristic of an early developing corpus luteum may be felt. The corpus luteum of the previous estrous cycle is usually palpable but small. A vaginal examination with

a speculum and light is often essential since the presence of hyperemia, relaxation of the cervix, and typical vaginal mucus of estrus is indicative of estrus; and the presence of blood in the vaginal mucus indicates that ovulation occurred one to two days previously. It is not unusual in examining a number of normal, well-nourished cows that have a history of failure of estrus to find one or more of these cows approaching, in, or just over, estrus. This fact may be missed by a hasty examination especially if a speculum examination of the vagina is omitted. Cows in proestrus, estrus or very early metestrus should be bred. Cows in metestrus after ovulation has occurred should be noted on the heat expectancy chart and watched closely 18 to 20 days later.

Cows in anestrus due to a failure of the estrous cycle caused by nutritive deficiencies or debility from other causes; cows with cystic ovaries; and occasionally cows with such miscellaneous conditions including freemartinism, hypoplasia of the ovaries, ovarian tumors, and pituitary disturbances comprise this group of cows.

(2) Anestrus secondary to debility or marked loss in weight. Any severe and chronic adverse or stress conditions that affect the animal's body will produce an effect on the reproductive system, usually by causing a cessation of the estrous cycle and anestrus if the animal is not pregnant; or in more severely debilitating conditions, possibly causing abortion if the animal is pregnant. Reproduction is a "luxury" function of the body. If "stress" due to any cause is severe enough, estrous cycles and reproduction cease. The adverse debilitating conditions that suppress or stop the estrous cycle and produce anestrus are:

(a) A low plane of nutrition due to a lack of sufficient intake of carbohydrates, proteins, and other elements necessary to maintain body weight may cause a failure or delay in the onset of puberty or the onset of the estrous cycle following parturition. Energy deficiency or negative energy balance is common in high-producing cows the first 20 days after calving. Ovulation and luteinization occurred about 10 days after the energy balance was returning to a positive balance. To prevent longer calving intervals in high-producing cows, feeding of large amounts of energy is essential early in the first third of lactation.^{23b} Cows exhibiting estrus before 30 days postpartum were more fertile with fewer services per conception, 2.29, than cows with no heats in this period, 2.63.^{89c} (See Nutritional Causes for Infertility.) This condition is seen most often in heifers maintained on poor hay or on poor pasture or range. The incidence of "winter sterility" in England characterized by anestrus varied from 5 percent around Cambridge to 50 percent in the Yorkshire Mountains, where cattle were kept in cold,

dark barns and fed poor hay.³⁸ Heifers fed on a high level of nutritive intake reached puberty and developed estrum at an average of 9 to 10 months of age, whereas heifers fed on a lower nutritive level did not reach puberty and estrum until 16 months or more of age.^{13,78} These latter heifers were maintained at optimum environmental conditions except for the level of feeding. The various nutritive factors that adversely affect the estrous cycle may also include severe nutritive deficiencies of phosphorus, cobalt, iron, copper and possibly other trace elements. When these substances are lacking, anorexia and debility, with impairment or suppression of the secretion of the gonadotrophic hormones by the pituitary, may develop. It is well known in humans that starvation causes amenorrhea and a cessation of the menstrual cycle before other body disturbances appear. In rats a loss of 15 percent in body weight may stop the estrous cycle. This was illustrated in cows during an experiment on the effects of a sodium chloride deficiency.¹ When this common element was withheld for long periods the effects became very evident after calving. Lactation caused rapid loss of weight because the appetite was poor. Milk secretion declined and ceased. The cows became cachectic and failed to show estrum. On examination the ovaries were found to be small and inactive; an occasional small 1 cm. follicle was palpated. Estrum did not return until salt was supplied and the appetite, nutritive state, and body condition improved.

Most practicing veterinarians have observed anestrus on farms where cows and heifers are thin and poorly fed. In a survey of 1533 cows in 28 herds in New York State, carotene, vitamin A, calcium, phosphorus, and iodine deficiencies did not contribute to sterility.⁴⁰ Inasmuch as reduced hemoglobin, below 9 gm. per 100 ml. of blood, was noted in all anestrus cows, cobalt and copper deficiencies may have been a factor. In heifers or cows that are in a fair state of nutrition but are exhibiting anestrus, the condition may be due to a simple phosphorus deficiency, or a phosphorus and a protein or carbohydrate deficiencies. A herd of dairy cattle deficient in phosphorus intake was described but anestrus was not observed in the deficient cattle in this herd.⁶¹ Blood levels below 3 mgm. percent usually indicate a phosphorus deficiency.^{61,92} Failure of estrum with non-functional, inactive or "smooth" ovaries is observed most often during the winter months in the northern part of the country in cows on poor and inadequate amounts of feed. In the southern and western part of the country where the animals are on pasture most of the year the condition is observed most commonly during the dry, late summer pasture season when available feed is greatly reduced. It may also be observed under drouth conditions. A de-

lay in the occurrence of estrus after parturition especially in range beef heifers on a low level of TDN or energy intake prior to or after parturition has been reported.^{4,13,21,97,98} This was also associated with a lower conception rate after estrus occurred. Heavy lactation, with or without ketosis, will often result in the rapid loss in body weight and if this is extreme, cessation of the estrous cycle will occur. If the loss in weight after calving is more gradual, an estrus or two may occur before anestrus develops. In lactating cows showing anestrus of nutritional origin, milk production is usually lowered. Anestrus due to low nutritive intake is usually characterized by the fact that a large number of cows or heifers on a farm show the same symptoms. Examination of 4 or 5 animals that fail to show estrus will usually reveal small, atrophic, inactive ovaries. (See Figure 117.) No corpora lutea are palpable. The uterus is usually small, lacks tone, and is doughy and flaccid. On vaginal examination the mucosa of the vagina and cervix is pale and dry. Repeated examinations reveal no change in the reproductive organs. The affected animals are usually thin and have rough hair coats and dry feces.

(b) Chronic or debilitating diseases, by causing a decreased appetite, may result in failure of estrus due to a marked reduction of body weight. Examples of these diseases or conditions include severe mange, lymphocytoma, severe chronic traumatic gastritis, chronic severe pneumonia, Johnes disease, actinomycosis that interferes with eating, either severe external or internal parasitisms, including liver fluke infection,^{33a} severe suppurative processes such as suppurative arthritis secondary to foot rot with a secondary severe debility, advanced tuberculosis, hyperkeratosis, anaplasmosis, and other similar diseases and conditions. If the cow recovers from the disease or its effects are alleviated and appetite and body condition returns, the estrous cycles will be reestablished.

(c) Senility or old age with loss of teeth and inability to masticate properly, especially in older lactating cows, is a cause of loss of weight, debility, and anestrus or failure of estrus. In extremely old cows, 16 years and older, anestrus may rarely be associated with a severe reduction in the number of oocytes in the ovary as in menopausal women.

(d) Seasonal influences—especially environmental temperatures, sunlight, and exercise apparently play a lesser role than does nutrition on the estrous cycle and estrus. Failure of estrus or anestrus in cattle has often been observed in cows and heifers closely confined in dark stables and allowed little or no exercise. This may be compounded by a lack of observation and a lack of proper care and nutrition. In the northern part of the

country where cows are confined during the winter months, even though the cow is polyestrous the best conception rates occur in May, June, and July whereas the poorest breeding months are December, January, and February. This is undoubtedly a reflection of the amount of sunlight and its effect on the pituitary as well as the feeding levels, amount of exercise, type of feed available and closeness of observation for estrus. During the cold winter months additional nutritive energy is required by animals to maintain body temperature and in heifers an added requirement is necessary for growth.

Excessive heat stress over long periods of time may cause anestrus, a shortening in duration and intensity of estrus and an increase in incidence of "silent" heats.^{89a,b} Five of 6 two-year-old heifers developed anestrus and cessation of the estrous cycle after being kept for 5 weeks at a temperature of 90° F and 60 percent humidity. Besides these effects on the estrus cycle and periods, excessive heat and humidity greatly lowers conception rates and production in dairy cows in tropical climates during the summer months. The use of shade, evaporative cooling and partial air-conditioning greatly reduces or alleviates these adverse effects of heat stress.^{89b}

(3) Cystic ovaries, as reported previously, are characterized externally by failure of estrus or anestrus in about 25 to 75 percent of the cases. On rectal examination one or more follicular or luteal cysts are found. The uterus is usually doughy and flaccid and may be atrophied. The mucus in the vagina is tenacious, and varying degrees of edema of the vulva and relaxation of the pelvic ligaments occur due to prolonged estradiol concentrations in the blood plasma. Treatment consists of injecting luteinizing hormone (LH) or GnRH or prostaglandins for luteal cysts. Some cases of mucometra are associated with cystic ovaries and long-standing anestrus. This condition might be confused with pregnancy unless a careful examination is made. Another rare condition the author considers as also associated with prolonged cystic ovaries and anestrus is characterized by a greatly enlarged and dilated cervix filled with copious amounts of tenacious, tough mucus similar to the mucus of a cervical seal of pregnancy. This latter condition may also have mucometra along with the cervical lesion.

(4) Miscellaneous conditions characterized by anestrus or failure of normal estrus with no corpus luteum are generally uncommon and sporadic in the United States. These may include occasional cases of:

(a) Non-functional or "smooth" ovaries may occasionally be observed in apparently well-nourished older cattle in good condition the first 2 to 4 months after parturition when the level of lactation is high. Cows stressed at the period of calving by the occurrence of a

disease process such as retained placenta, dystocia, milk fever, ketosis, mastitis, twins and other debilitating diseases had a delayed onset of the estrous cycle of an average of 34 days compared to 15 days for cows with a normal parturition. Seven percent of the cows and 3.99 percent of the estrous cycles studied were characterized by a varying period of anestrus with "smooth" or non-functioning ovaries.⁹¹ The uterus is flaccid and lacks tone. Spontaneous recovery usually occurs. This condition is probably due to a reduced level of nutrition associated with a definite loss in weight. When production and energy intake are equalized, the estrous cycle will occur.

(b) Freemartinism may be a rare cause of anestrus in heifers purchased from unknown sources or raised by farmers who did not know that 90 percent of heifers born cotwin to bulls are sterile. These freemartins are usually steer-like in appearance. They have a small vulva with a coarse tuft of hair and a prominent clitoris. On rectal examination the uterus and ovaries usually cannot be palpated except as thin or small remnants of the normal structures. Vaginal examination will reveal an undeveloped vagina cranial to the vestibule.

(c) Congenital bilateral hypoplasia of the ovaries is rarely observed in the United States. Several related cattle were described with a complete absence of gonads.²⁷ In rare instances, heifers may have a fairly normal but small infantile genital tract but very hypoplastic, small, flattened, slightly corrugated ovaries the size of a bean or smaller 0.5 to 2 cm. long and 0.25 to 0.5 cm. in diameter. (See Figure 118.) These hypoplastic ovaries may be observed either unilaterally or bilaterally. Heifers unilaterally affected or those with partial hypoplasia of an ovary usually have normal estrous cycles. Small, inactive, immature ovaries 0.5 to 1.5 cm. in diameter; especially in prepubertal heifers, may erroneously be diagnosed as hypoplastic ovaries. Heifers should be in good physical condition with no obvious cause for the small inactive ovaries and be old enough to have estrous cycles before a diagnosis of congenital hypoplasia should be considered. In a few of these congenital or hereditary cases of hypoplasia, the uterus and oviducts on one or both sides may also be hypoplastic. In the United States congenital, or possible hereditary, bilateral total hypoplasia of the ovaries is rare and sporadic. In Sweden, widespread hereditary ovarian and testicular hypoplasia were formerly present in the Swedish Highland breed of cattle.^{26,53} Inbreeding has been associated with the development of this defect as with other hereditary anomalies of development.

(d) Tumors of the ovary are rarely noted as a cause of anestrus or failure of estrus. In the cow the most common tumor is the granulosa cell tumor that may cause



Figure 118. Bilateral Total Hypoplasia of the Ovaries in a 3-year-old Holstein.

occasional symptoms of either nymphomania or anestrus. The early stages of these tumors usually pass unnoticed and by the time clinical symptoms of pelvic relaxation, edema of the vulva, and others are evident, rectal examination will reveal the nature of the condition by the presence of an abnormally large ovary, 7.5 cm. or more in diameter, usually pulled forward and downward in the abdominal cavity. The ovarian artery to the diseased ovary is usually enlarged. Removal of the diseased ovary may be indicated in some cases. Several authors have reported finding granulosa cell tumors in related cattle. Rarely chronic tumors, abscesses and cysts in the ventral area of the brain affect the pituitary gland by causing pressure atrophy and a deficiency of gonadotropic hormones, thus producing cessation of the estrous cycle and atrophy of the gonads. Large and prolonged doses of the gonadal hormones, estrogens, progesterone

and testosterone, whether taken orally or by injection will suppress the release of gonadotropic hormones and result in smooth, inactive, nonfunctioning, atrophied ovaries. Anestrus due to this cause is also rare in cattle.

Treatment of anestrus in cows that have no palpable functional corpora lutea and in which the plasma progesterone levels are continuously low, or occasionally high as in luteal cysts, will vary with the clinical findings. Anestrous cows with cystic ovaries containing follicular or luteal cysts should be treated in ways described under cystic ovaries. Heifers or cows with freemartin genital tracts, bilateral total ovarian hypoplasia, which should not be confused with infantilism or failure to reach puberty, very rare absence of the gonads, ovarian tumors, or rare lesions of the pituitary gland or the hypothalamus should be slaughtered as treatment is not indicated or successful. Removal of one ovary affected with an ovarian tumor, especially a granulosa cell tumor, may rarely restore fertility to the heifer or the cow. In the case of unilateral ovarian hypoplasia the strong possibility that the condition is genetic in nature should be seriously considered. If ovarian atrophy or cystic ovaries are due to exogenous estrogens, or possibly progesterone, testosterone or progestagens, these should be removed from the diet or the ration changed or injections of the same should be stopped. It may take from a week to several months or more before the estrous cycle is reestablished.

Treatment of anestrus due to debility, cachexia or a lack of TDN (energy), protein, or other minerals should follow a careful clinical examination and diagnosis often requiring an analysis of the feed. If the cause is due to chronic debilitating diseases these must be corrected or alleviated so the female returns to a good condition with near normal body weight. Additional levels of TDN and other nutrients need to be fed to these animals. Therapy may require a number of months. In senile animals the prognosis is poor but occasionally pelleted, easily digested feed may be helpful.

Treatment of anestrus due to a low level of nutrition is obviously corrected by greatly increasing the nutritive levels. Since many farmers refuse to recognize they are underfeeding and mismanaging their stock, particularly heifers, this is a difficult or impossible problem to correct in some herds. Frequently nature corrects it in the spring when the animals are turned out to pasture where the feed is excellent and unlimited; the weather is warmer; the days longer; and exercise is plentiful. Occasionally a farmer or owner can be persuaded to accept your diagnosis and suggested treatment on a trial basis by taking several anestrous heifers with small functionless ovaries and placing them in the barn with the milking cows and

feeding them as if they were cows producing 50 lbs of milk a day. In 3 to 6 weeks these heifers usually come into estrus while their less fortunate companions—fed less and on a poor quality feed and usually kept in a colder and less favorable environment—remain anestrus. This same problem may be observed in certain areas of the country and in certain beef herds where there are deficiencies of either one or more minerals such as phosphorus, cobalt, iodine, copper, salt, iron, and others, and/or of total digestible nutrients. Often nutritional deficiencies producing cessation of the estrous cycle are multiple. In some high producing old cows that are very thin and poor and are persistent milkers, it may be advisable to stop lactation to enable them to gain enough body reserves so that estrous cycles will begin again. Good pasture is desirable. Estrus will not occur in these debilitated animals until they receive feed over and above the requirements for maintaining life and are in a positive energy balance. In heifers or cows in a fair to good nutritive state but failing to show estrus because of a phosphorus deficiency, steamed bonemeal or dicalcium phosphate should be fed free choice. Complex mineral supplements or specific mineral supplements may be necessary, free choice or incorporated into the salt or feed in anestrus, mineral-deficient cows with a low blood hemoglobin level.

In range beef heifers and cows the delay in the onset of puberty or estrus after calving, especially in nursing two-year-olds and the lowered conception rates have been described.^{13,79,97,98} These studies have demonstrated the importance of feeding proper supplemental levels of nutrients, especially energy and phosphorus to heifers and two-year-old cows after calving. The value of vitamins for the treatment of anestrus in range cattle is questionable.

Miscellaneous Infertility Conditions Possibly Associated with Hormonal Disturbances

Hormonal therapy for cows that are cycling regularly but fail to conceive has been used empirically in the past by many veterinarians. If the therapy has not been coupled to a careful diagnosis of the etiology of the repeat-breeder cow which is difficult, results are usually unsatisfactory or conception occurs despite the treatment. The use of luteinizing hormone (HCG) or GnRH to promote ovulation has been described but failure of ovulation or delayed ovulation only occurs occasionally. HCG may also be used about the third or fourth day after estrus to promote the growth and increase the size and



Figure 119. A "Smooth," Inactive Ovary Seen Bilaterally in Debilitated or Thin Heifers and Cows and Causing Anestrus.

progesterone production of the corpus luteum but its value has not been evaluated in controlled studies. Veterinarians have also suggested the use of repositol progesterone, 500 mg. a few days after breeding⁷¹ but controlled studies are also lacking. The use of small doses of estrogen or GnRH early in estrus to promote the release of LH and ovulation has not proven to be of value except possibly in a few special cases in cows in which early embryonic deaths apparently occur. F.S.H. is not indicated in cycling infertile cows or in non-cycling cows. Thyroid therapy in the form of iodinated casein (**Pro-tamone**) 1 gm. per 100 lbs. body weight orally daily, 5,000 to 15,000 mg. triiodothyronine (**Cytomel**, Smith Kline and French) in pellet form subcutaneously or 2 to 5 grains of thyroid orally daily has been used for anestrus. It has also been used empirically for infertile cows or heifers, especially those that are obese or have become steer-like in appearance. Thyroid preparations should not be used in thin cattle in which anestrus is due to a lack of T.D.N. or energy intake. A possible abnormal steroid metabolism in inbred Jersey cattle characterized by delayed puberty, a short estrus, irregular cycles, failure of conception and decreased secretion rate of sex steroid and cortisol has been described.²⁴ Controlled studies in infertile cattle with the above hormones is probably indicated to prove or disprove their value. It is unlikely they will be proven to be of value unless better diag-

nostic tests are developed so that the use of hormones becomes based on scientific, sound information.

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Infertility Due to Nutritional Causes

During the past 30 years a great mass of knowledge has accumulated about the effects on animals of various nutrients and their deficiencies. Since much of the early

work was done on the rat and on laboratory animals, some nutritional fallacies have developed in so far as they pertain to domestic animals. The effect of nutrition on reproduction, sterility, and infertility has not been discussed but the relation of nutrition or nutritive deficiencies to abortion and anestrus has been reviewed in Chapters VIII and XIII. Excellent reviews on this field have been published.^{1,20,25,30,31,37,41–44} Only a few nutrients have a direct effect on fertility. Some infertility conditions blamed on nutrition may in reality be due to other related or nonrelated causes. Most field cases of reduced fertility or of sterility of nutritional origin are usually due to multiple deficiencies. Underfeeding may be accompanied by poor quality of feed and by deficiencies of protein, phosphorus and vitamin A. A protein deficiency is usually accompanied by a phosphorus deficiency, and a vitamin A deficiency by a protein and phosphorus deficiency. Sometimes reduced fertility believed to be of nutritional origin may be caused by the amount of light, environmental temperature, amount or type of work, or some other environmental influence. More work is required in this field as much of our present data is based on poorly controlled experiments and too few observations. It has been found that nutritional data accumulated on one species of animal does not always apply to other species. Symptoms of a certain deficiency in one species may differ from those in another species. At one time or another claims have been made that every known food factor is indispensable for normal reproduction.⁴¹ In so far as reproductive performance is based on the general health of the animal this may be true. Malnutrition leads to lowered vitality and lessened resistance to disease but proof of such effects on the reproductive system are few and all too often not conclusive. If disease is complicating the malnutrition then corrective efforts must be directed at both conditions. Lactation, however, places a heavy drain on an animal already deficient especially in certain minerals and in the general level of feeding. Specific deficiencies seldom cause specific lesions in the reproductive system. Infertility or sterility due to nutritional causes is usually characterized by a cessation of the estrous cycle and only under certain conditions is it characterized by a failure of conception or early embryonic death. Reproduction is a “luxury” function of the body. When body functions and needs are severely compromised, reproduction usually is the first system affected and if adverse influences are continued, reproductive functions cease.

Underfeeding, inanition, or starvation has been shown to delay sexual maturity in heifers^{30,37,44} and to inhibit estrous cycles in mammals of all ages. When dairy heifers were fed various levels of TDN from birth to first

calving equivalent to 62, 100 and 146 percent of the upper level of Morrison's Feeding Standard, the average age at the onset of puberty was 88, 49, and 40 weeks. The body size at the time of puberty was the same for all feeding levels. When the energy intake in the adult animal is low, follicles fail to develop to maturity and follicular atresia results, along with a loss of sexual desire, anestrus and cessation of the estrous cycle. Restricted food intake may have an effect on the early embryo but starvation after this period does not necessarily interrupt gestation but may cause stillbirth or birth of small, weak young.³¹ It is nearly impossible to conduct an experiment on a single food deficiency without encountering a partial inanition in animals. Under-feeding or inanition is seen in cattle most commonly during the winter months when they are confined and/or the quality and quantity of the feed is limited or reduced. In older cattle irregular estrous periods and anestrus are manifested as a result of underfeeding. Inanition reduced the secretion of gonadotropic hormones and other hormones by the anterior pituitary although the gonadotropic levels in the pituitary were normal.^{31,37} The fact that the ovaries remain responsive to stimulation by gonadotropes during under-feeding does not mean that normal estrous cycles and pregnancy could be maintained by administration of hormones, since undernutrition probably exerts a direct effect on the reproductive tract although the major effect is on the endocrine glands.

It has been shown in primiparous beef heifers that energy intake levels before and especially after calving and during lactation have a marked effect on the occurrence of postpartum estrus and conception rates.⁵⁷ In beef heifers fed high TDN, 9 lbs. and low TDN, 4.5 lbs. daily before calving and then high TDN, 16 lbs., and low TDN, 8 lbs. daily after calving the conception rate for 20 heifers in each group was High-High 95 percent, High-Low 77 percent, Low-High 95 percent and Low-Low 20 percent. The percentage of cows cycling by 60 days postpartum was 80, 81, 45 and 17 respectively in the four feeding groups. Thus it is more important that cows suckling calves receive more energy than pregnant animals.^{56,58} The birth weight of calves from cows on the low energy ration during pregnancy was 10 lbs. lower on the average than the weight of calves from cows on the high energy ration, 67 lbs. vs 78 lbs. Beef heifers should be fed to gain one pound a day from weaning through the breeding season.⁵⁷ Heifers of the English breeds of cattle should weigh 650 lbs. at the start of the breeding season. Beef cattle should be in good condition at calving and should be fed to gain 0.5 to 0.75 lbs. per day after calving until the end of the breeding season to avoid low reproductive performance. In a herd of 327

beef cattle free of infectious causes for infertility the conception rate dropped from 87 percent to 41 percent, 28 percent in lactating and 76 percent in nonlactating cows, under drouth conditions.⁹ Injections of vitamins A, D, and E during the breeding season failed to improve the conception rate. A higher incidence of dystocia in heifers was reported on a below normal energy intake during the gestation period.⁴⁴ Retarded early growth in cattle due to a low plane of nutrition was associated with a prolongation of the life span.⁴³

Evidence indicates that animals come into estrum and conceive most readily when their body weight is rising due to an increased plane of nutrition and conversely a low pregnancy rate occurs in beef and dairy cattle losing weight during the breeding season.^{12,13,21,23,30,36b,57} In 179 Ayrshire cows on 3 farms that were weighed every 4 weeks and serviced not less than 56 days postpartum, 98 cows whose body weight increased after calving had a 77.6 percent conception rate on first service while 81 cows whose body weight decreased had a 16 percent conception rate on first service.²³ There was no correlation between conception rate and milk yield. New Zealand studies showed that cows gaining weight had similar conception rates to those that lost only a modest amount of weight after calving.³⁴ It was also noted in Israel that a positive energy balance if achieved fairly promptly after calving resulted in an improved conception rate.²¹ They suggested that weighing cows at intervals after calving might be helpful in determining the need for increased energy intake and in determining the time for insemination. (See Anestrus.) The dairy and beef herd infertility syndrome associated with a negative energy balance and loss of weight was described^{12,30} to include: (1) low first service nonreturn rates; these are seldom below 30 percent, (2) spontaneous recovery but many cows are not pregnant by the third month after the first service, (3) affected cows lose an excessive amount of body weight, 5 to 10 percent, between calving and first service; such a loss is often not obvious, and (4) low blood glucose, hypoglycemia, is frequently observed in infertile cows at the time of the first service. The estrous cycle length was increased from normal to 34 days when cows were given insulin daily from day 17, but not day 18, through day 20 of the cycle.²⁹ In 11 cows mated 0 to 2 days after the last dose of insulin only 2 or 18 percent were pregnant at 8 weeks, and of 16 cows given insulin, 400 units daily the first four days after mating only 6 or 38 percent were pregnant at 8 weeks. While 15 of 20, or 75 percent, of the control cows were pregnant. Thus it is possible that a hypoglycemia at estrus and shortly after service may exert a harmful effect on conception. This effect may be brought

about by a lowering of the glucose or glycogen levels in the mucosa of the genital tract resulting in a lack of energy for spermatozoa and embryos. Further study of these interesting observations are needed. Reproduction in Herefords was more severely affected by low levels of TDN intake after calving than in Angus cattle.¹³ Weight gain in yearling heifers during the prebreeding period caused by "flushing" or feeding high energy rations was more important in its effect on age at puberty than was the gain during the wintering period.⁷ Thus it appears important that feeding practices in dairy and beef herds be such that, despite the stress and energy requirements of lactation, cows to be bred should be in a positive energy balance and gaining weight as soon after calving as is possible to realize the best breeding results.

Obesity due to overfeeding has been considered by many practicing veterinarians to be a cause of infertility in cattle. This is observed particularly in the beef breeds and has often been reported to affect valuable show cattle. Early references indicated erroneously that in these overly-fat animals the ovaries are small and estrus may fail to occur.^{1,56} Obese, over-conditioned dairy cows are prone to the "fat cow syndrome" at calving (see post parturient diseases). The diseases associated with this syndrome have an adverse effect on fertility and often greatly prolong the period from calving to conception.^{36b} Obesity and sterility might arise from the same cause such as hypothyroidism or from a pituitary lesion. Fat deposits in the ovaries and ovarian bursae were suspected of interfering with normal ovulation and transport of ovum to the oviduct. Recent nutritional research has not confirmed the observation in cows that obesity and infertility are associated. Reid stated, "It is as logical to assume that sterility is the cause of high condition as it is to assume the reverse."⁴³ In a rather large controlled experiment animals kept on a high plane of nutrition their entire life had fewer calves and a higher percentage of culling due to infertility than did the animals fed at normal and low levels of nutrition.³⁸ Swedish data, New Zealand reports, and experiments at Cornell,⁴⁴ indicated that heavy feeding hastened the onset of puberty, caused a slight increase in number of services per conception if heifers were withheld from breeding for a number of months after reaching puberty; and resulted in lower milk yields and a shorter life. Cattle reared on a high plane of nutrition had more breeding difficulties later in life and thus had a shorter productive life than cattle reared on a low energy intake.⁴³ A high level of grain feeding of up to 4790 kg per lactation over a period of years in dairy cows had no significant effect on conception rate.⁶ Fat heifers and cows with large deposits of perivaginal fat may have more difficulties at parturition. The problem of the effects of overfeeding on reproduction in cat-

tle is not settled and more controlled experiments are needed and indicated.

Protein deficiencies of either quality or quantity under the usual conditions of management of cattle are not common. Although the quality and quantity of protein might be important for reproductive functions, deficient amounts are seldom encountered except in severe inanition or underfeeding when vitamin A and phosphorus deficiencies are often complicating factors. The effect of a low level intake of protein on reproduction may be to reduce the total intake of feed, resulting in a delay in estrus.⁵⁶ The high content of phosphorus rather than protein may explain why cottonseed meal is a better supplement for beef cattle in the Southwest than is grain during the winter months.²⁴ Pelleted alfalfa fed at a rate of 2 to 5 lbs. daily per animal is an excellent protein supplement. The level of energy intake is more important for reproduction than is protein.

Vitamin deficiencies in cattle are mainly limited to vitamin A. Deficiencies of the other vitamins are not likely to cause reproductive failure.

Vitamin A deficiency adversely affects reproduction in most species. The effects occur during the latter half of gestation and are characterized by abortion or by the birth of weak or dead calves (See Abortion, Chapter V). It seems remarkable but it is nevertheless true that vitamin A deficient animals have normal estrous cycles, ovulate and conceive, and early fetal development occurs even though epithelial and other tissue changes have developed. Infertility in cattle and other domestic animals has not been associated with vitamin A deficiency or with a deficiency of the other vitamins.

In the mid to late 1970's many articles were published in Europe on the beneficial effects of beta-carotene on bovine fertility. Beta-carotene and vitamin A are deficient in corn silage.^{10,20} Supplementing such diets with 200,000 IU vitamin A and 300 mg. beta-carotene per head per day reduced the time from calving to conception, reduced the incidence of ovarian cysts and reduced embryonic deaths, early abortions and disease prone calves.^{20,27} The bovine CL contains beta-carotene but no vitamin A. The former can be converted into vitamin A. Evidence would indicate that vitamin A provided by good hay, especially alfalfa, and pasture should provide the vitamin needs for reproduction.¹⁹ The present requirement for vitamin A in dairy cattle is 3,400 IU or 8.5 mg of carotene/100 lbs. of body weight.¹⁰ Experiments are now being conducted to determine whether greatly increased amounts of beta-carotene are needed for reproductive efficiency. Recent reports do not support the early claims for beta-carotene supplementation.^{58b}

Vitamin A requirements during pregnancy are higher than in the nonpregnant animal and higher for the female

than the male animal. Vitamin A deficiencies are characterized by changes in the epithelial tissues, such as keratinization and degeneration of the placenta. Fetal death, abortion, dystocia, retained placenta, and septic metritis are likely to result. Vitamin A deficiency has been described in cattle grazing dry, bleached pastures and grain fields where possibly protein, phosphorus, and carbohydrate intake were also deficient. When green feed became available, night blindness, lacrimation, anorexia, diarrhea, loss of condition and other general symptoms of vitamin A deficiency, as well as abortions and stillbirths, ceased. The liver has the ability to store considerable amounts of vitamin A for some time; therefore symptoms of vitamin A deficiency take months to develop. Good timothy hay has a much lower content of vitamin A than does alfalfa hay. Under most conditions where roughage is of average quality, vitamin A deficiency is very unlikely to occur and even then the reproductive effects are not those causing infertility in the cow.

Vitamin B or B-complex deficiencies have been demonstrated in animals as producing the same inhibitory effects on reproduction as reduced food intake or starvation. This is not unexpected, as deficiencies of B vitamins are usually accompanied by a reduced appetite. By virtue of ruminal synthesis of these B-complex vitamins, cows are in no danger of suffering from vitamin B deficiencies. One of the B-complex vitamins, vitamin B₁₂, requires cobalt in its synthesis; cattle in cobalt-deficient areas may develop severe inanition due to lack of sufficient intake of feed occasioned by a cobalt and B₁₂ deficiency and a lack of appetite.

Vitamin C deficiency does not occur in cattle; only man, monkeys, and guinea pigs manifest symptoms of vitamin C deficiency, or scurvy, and even in these species no reproductive disturbances are produced when severe scurvy is present.

Vitamin D deficiency probably seldom occurs, due to the presence of vitamin D in roughage of almost any quality. If the animal gains access to sunlight or green pasture, adequate amounts are available. An uncomplicated vitamin D deficiency does not interfere with reproduction in mammals.³¹

Vitamin E deficiency, like vitamin A deficiency, does not affect the estrous cycle or ovarian function. In deficient rats pregnancy is interrupted after midterm by resorption of the fetuses. In the male rats vitamin E deficiency irreparably damages the seminiferous epithelium giving rise to its early name—the “antisterility” vitamin. In herbivorous animals it is doubtful that a need for vitamin E for reproductive purposes is greater than the quantity liberally present in the natural feed. Cows can reproduce on a vitamin E deficient diet. Heifers and bulls

receiving vitamin-E-deficient diets were fertile.¹⁵ In the past, extravagant claims have been made for the use and value of vitamin E supplementation of rations in the treatment of all types of reproductive disorders in cows and bulls. These claims and reports, largely commercially-developed and exploited, were uncontrolled. The use of wheat germ oil in cases where spontaneous recoveries of infertility are known to be high resulted in a great number of apparent “cures” with this product. Reports on more carefully controlled data and experiments using wheat germ oil or sprouted oats showed no difference in results between the treated and the control groups of cattle. At the present time vitamin E therapy for infertility cannot be recommended since it is of no known value.

Mineral deficiencies causing infertility in cattle are limited mainly to phosphorus and occasional trace minerals. Trace minerals in cattle nutrition have been reviewed.⁵

Phosphorus deficiency usually tends to occur when diets low in protein are fed, under range conditions when the grass is dry and dead, in areas where the soil is deficient in phosphorus, and in borderline phosphorus-deficient areas when the cows are lactating and are not fed sufficient protein or mineral supplements to maintain the necessary body levels of phosphorus. Until clinical symptoms of the deficiency, such as inanition, poor hair coat, and depraved and decreased appetite are evident, reproduction usually does not suffer. In some phosphorus-deficient areas cows had calves only every 2 years, and heifers failed to show estrus until over 2 years of age. The condition was most severe in the late winter and spring after a dry summer and fall. Some cows would have one or two periods of estrus after calving and then if they failed to conceive would not show estrus until the end of the lactation period. “Silent” or irregular estrus periods may occur in heifers. Thus the usual symptoms of phosphorus deficiency are delayed onset of puberty in heifers, and failure of estrus in cows. The relationship between phosphorus deficiency and infertility in dairy cattle was reviewed.³⁶ With proper phosphorus supplementation the number of services required for conception declined from 3.7 to 1.3 in dairy heifers suffering from a phosphorus deficiency. The Ca:P ratio, especially excess Ca to P., could influence fertility but this was not confirmed.^{17,18,26}

The phosphorus requirement for reproduction is about 10 to 12 gm. daily except during lactation when an additional amount is required.¹ Blood levels of phosphorus below 4 mg. per 100 ml of blood serum usually indicate a phosphorus deficiency; normal values are 4 to 8 mg. per 100 ml. Phosphorus levels are much lower in timothy hay than in legumes. In states where phosphorus

deficiency is common, the feeding of mineral supplements or cotton seed meal has resulted in marked improvement or increases in the yearly percentage of calves born. Mineral supplements to supply phosphorus include dicalcium phosphate or bone meal and these should be available free-choice together with trace mineralized salt for all cattle. Adding 1 percent sodium tripolyphosphate or monosodium phosphate to the grain ration will also increase the phosphorus intake.³⁶ **Calcium deficiency** does not cause reproductive failure in cattle.

Other trace element deficiencies, that may affect reproduction indirectly, are: **Manganese**—In cattle there are few reports of naturally-occurring manganese deficiencies. It appears nearly impossible to devise an otherwise normal ration for cattle that is deficient in manganese.^{42,43} However, reduced conception rates and anestrus in cattle deficient in manganese that was corrected by manganese supplementation was reported.^{30,45,54}

Cobalt deficiency in certain areas may cause a lack of appetite, depraved appetite, inanition, secondary failure of estrus, and delayed onset of puberty in cattle. Low hemoglobin values were observed in many anestrus animals. Cobalt is necessary for normal bacterial growth in the rumen. It is concerned in the production of vitamin B₁₂, which is an important factor in maintaining the appetite. In cobalt-deficient soils, legumes usually contain sufficient cobalt; but timothy hay produced on these soils is deficient in cobalt. **Copper and iron** deficiencies in some areas of the United States result in, or are complicated by, anemia, debility, lack of appetite, and consequently a reduced intake of feed. As with cobalt deficiency a secondary inanition, a failure of estrus, and a delayed onset of puberty may occur. The apparent association of anemia with hemoglobin values below 10 gms, especially in the range of 8.0 to 8.5 gms, per 100 ml of blood, and anestrus, delayed postpartum breeding and possibly repeat breeding have been reported upon in dairy cattle.^{2,52} In some cases this anemia has been related to low iron or copper levels in the forage. In certain areas such as some locations in Florida, a high molybdenum content in the feed results in severe scouring and loss of condition when copper is not added as a supplement in the feed. This loss of condition may be reflected in failure of estrus in cows or in the delayed onset of puberty in heifers. Copper-deficient cattle in New Zealand, England, South Africa and Australia,^{3,11,50,53} have marked general effects of lowered body health, loss of condition, slow growth and rough hair coat with secondary reproductive symptoms of failure of estrus, delayed conception, and infertility.

Iodine deficiency especially in the northern and north-

western parts of the United States may cause the birth of weak, premature or dead calves affected with goiter. Iodine is not known to affect reproductive processes. However, a lack of iodine can depress thyroid function.³¹ Hypo- or hyperthyroidism may reduce the secretion of gonadotropic hormones by the pituitary. An increase in conception rate was reported on first service and reduced irregular breeding intervals in herds in Finland receiving supplementary iodine compared to control herds.³³ In iodine-deficient areas iodine is usually provided in the salt. Severe salt deficiency over a long period of time, especially during lactation, will result in severe loss of body weight and anestrus.⁴⁶ **Zinc and selenium** has been shown to be closely associated with reproduction in laboratory and other animals but deficiencies in the large domestic animals have not been described.

Treatment of cattle with nutritional deficiencies is essentially one of prevention. In most deficiency areas these deficiencies are known and should be provided for by supplementing the ration. In most areas where cattle raising is profitable, deficiencies are usually uncommon in cattle fed near-normal or balanced rations. Usually general inanition, debility, and other symptoms are evident before reproductive symptoms develop. In most herds expensive mineral supplements are not necessary. Mineral supplements are added to the grain ration at a usual rate of 1 to 1.5 percent for dairy cattle. In certain mineral-deficient areas and in heavily lactating cows additional amounts or specific mineral supplementation such as magnesium may be necessary. A suitable mineral supplement for dairy areas in the northeast and middlewest consists of 86 lbs. of steamed bone meal or dicalcium phosphate, 12 lbs. of anhydrous ferrous sulfate, and 1.4 lbs. of copper sulfate and 1 ounce of cobalt sulphate or cobalt chloride. This can be fed free choice or added in small amounts, 1 ounce daily, to the grain ration.² If rock phosphate is used it should be carefully defluorinated to prevent possible fluorine poisoning. Chronic subclinical fluorine poisoning induced by feeding 5 to 12 ppm flourine in the drinking water caused anestrus, reduced conception rates and a drop in the pregnancy rate.⁵¹ In some cases subcutaneous injections of 1 to 6 mg. of vitamin B₁₂, 10 ml of iron dextran or 300 mg of copper glycinate may be given as needed if feed supplements are difficult to provide. There are few nutritional factors other than underfeeding that have been shown to have a widespread serious influence on reproductive functions. Trace elements had little if any effect on repeat breeding cows.⁸ Additional work, adequately planned and controlled, might profitably be applied to this problem of nutrition and fertility.

Miscellaneous nutritive, reproductive problems, especially infertility, may be associated with the consumption of excess estrogens from pasture plants especially during lush growing season. High estrogenic content of red clover, of alfalfa, subterranean clover and of ladino clover and other phytoestrogens have been reported upon.^{4,14,20,22,49,59} Infertility in cattle consuming such forage has been reported in isolated areas. Heavy kale feeding caused a reduced conception rate and prolonged intervals between estrous periods after service.^{32,39,40} No estrogens were found in kale but evidence of a goiterogenic factor was noted. Blood copper and hemoglobin were lower in kale-fed cows.³² Estrogenic mycotoxins or fungal metabolites may be a cause of infertility in cattle as they are in swine (See Chap. XVI) but evidence for this in the veterinary literature is scanty.^{8b,45b}

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Congenital or Hereditary Causes of Infertility in Cows

Congenital or hereditary causes of sterility or infertility may be divided into those produced by definite anatomical defects of the reproductive organs, cytogenetic defects and those hereditary forms of infertility that are obscure, possibly due to multiple factors and difficult to assess. Because of the rapid advances in recent years in the control and elimination of many infectious venereal causes of infertility the genetic causes of infertility are assuming greater importance. Excellent reviews of this subject have been made.^{15,18,26,36,53,72} Many breed associations and artificial insemination centers have programs for monitoring and controlling undesirable genetic traits.³⁶

Hereditary or Congenital Anatomic Defects of the Reproductive Tract

Hereditary defects are usually due to single gene effects. Certain genes adversely affect both cows and bulls whereas others are sex-limited in their effect. In some females because of the severity of the abnormalities, sterility is manifested at the time of their first service period; while in other cows, in which the defect is less severe, it may not be detected until late in life.

Hypoplasia of the ovaries and testes has been well described.^{9,10,32-35,55-57} This defect is conditioned by a single recessive autosomal gene with incomplete penetration. This gene affects both cows and bulls in equal proportions. The affected ovary may be partially or totally hypoplastic. Depending on the severity of the hypoplasia and whether the condition is unilateral or bilateral, infertility or sterility will result. (See Figure 118.) In the latter instance the affected heifer is anestrus. The origin of this condition in the polled Swedish Highland breed of cattle traced back to two bulls born about 1900. Through extensive use of these bulls and of their offspring because of the high-butter-fat production of these

individuals, the condition was spread widely. In cows with hypoplastic ovaries, 87.1 percent were left-sided, 4.3 percent were right-sided and 9.6 percent involved both ovaries. This condition can be recognized in the affected Swedish Highland heifers by rectal examination as early as 9 months of age. The incidence of partial or transitional hypoplasia occurred in about the same percentage as the total hypoplasia of the ovaries or testes. These intermediate conditions can be evaluated only by repeated rectal examinations of the ovaries over a period of time or at the time of slaughter. The hypoplastic ovary undergoes incomplete development and a part or the whole ovary lacks a normal number or complement of primordial follicles. Both ovaries of normal heifers contained a total of 50,700 primordial follicles, range 6,800 to 100,000. Both ovaries, in affected heifers in which one ovary was totally or partially hypoplastic averaged 19,000 to 23,000 primordial follicles.⁵⁷ In affected heifers with bilateral hypoplasia there were fewer than 500 primordial follicles in partially affected ovaries and no follicles were present in the heifers with totally hypoplastic ovaries. In heifers the hypoplastic ovary is so small that it may be difficult to locate. It is a thin, narrow, structure of firm consistency, or in severe cases only a cord-like thickening in the cranial border of the ovarian ligament. The ovary has a shriveled or shrunken appearance affecting the entire ovary in total hypoplasia (See Figure 118) or usually the medial half or two-thirds of the ovary in partial hypoplasia. In other cases one-half of the ovary feels slightly raised and firm like a pea. In other cases the ovary of an adult cow may feel like a kidney bean with the surface smooth and stretched. If the surface of the ovary is rough due to luteal scars the ovary can be considered functional. In one-sided hypoplasia the tubular portion of the genital tract develops normally. In bilateral total hypoplasia the genital tract remains very small and infantile; estrum does not occur and there is no development of the secondary sex characteristics due to a lack of estrogens. In bilateral total hypoplasia the heifer is like a steer with long legs, a narrow pelvis, a poorly developed udder with small teats, and a small, firm uterus. In bulls similar hypoplastic changes affect the testes. Swedish Highland cattle that were totally white or had nearly completely white ears included in their number all cows with hypoplastic ovaries.⁵⁵ Those with black or red ears were not affected. Thus the degree of white color was associated with hypoplasia.

Through efforts of the Swedish government, the breed association, owners, and veterinarians, a campaign to control this condition has been established by culling affected animals. The incidence of this condition has dropped from 17.5 percent of the cattle in the Swedish

Highland breed in 1936 to 9.4 percent in 1948. In 1952 based on the examination of the genital organs from 6286 Swedish Highland cattle the incidence of hypoplasia of the left ovary was found to be 6.6 percent, right ovary 0.5 percent, and of both ovaries 0.09 percent; a partial hypoplasia of the left ovary of 3.3 percent, of the right ovary 1.1 percent, and of both ovaries 1.6 percent; or an incidence of total hypoplasia of 7.2 percent and partial hypoplasia of 6.0 percent. The incidence of this condition was severe enough in certain areas of Sweden that it resulted in a great increase in the incidence of right horn pregnancies which in 1939 was reported to be about 74 percent.³⁰ At the rate of decline in the incidence of the defect observed between 1936 and 1952, it would take more than a century to reduce it to less than 0.5 percent—a striking demonstration of the insidiousness and seriousness of some hereditary defects! The incidence of gonadal hypoplasia in cattle in Sweden had leveled off and remained about the same from 1954 to 1964.⁵⁸

Hypoplasia of the gonads is not known to occur in any hereditary pattern nor in any particular breed in the United States. The condition was described in 59 of 2935 Cows or heifers.⁶⁶ An incidence of 1.9 percent ovarian hypoplasia was reported in over 20,000 cows examined in Minnesota.⁷³ Several cases in closely-related Shorthorn cattle were described.¹⁷ Many other veterinarians including the author have observed occasional cases of unilateral or bilateral, total, partial or transitional hypoplasia in cows. The rare cows with bilateral total hypoplastic ovaries are sold as sterile but the danger of breeding the unilaterally or partially affected cattle should be seriously considered, and slaughter probably advised. In ovarian hypoplasia treatment with hormones is useless. The condition of hypoplasia should be differentiated from nonfunctional or atrophic ovaries in cows and small, inactive ovaries in heifers associated with a delayed onset of puberty due to inarition or underfeeding.

A gonadless condition or lack of one or both gonads has been described in cattle.^{14,33} The latter reported one case of a uterus unicornis in which only one ovary was present. The condition of a complete failure of development of gonads occurred in 3 heifers from the same dam sired by different bulls. The dam was inbred. The cow had 2 normal daughters; one was a twin and the other a full sister of 2 of the gonadless daughters.¹⁴ This was probably an inherited autosomal dominant.¹⁸ These gonadless heifers appeared normal until breeding age, but no estrum occurred and normal udder development was lacking. The genital tracts of these heifers were juvenile and undeveloped. Another case of a gonadless heifer, not related to the previous ones, was cited in which mucometra was present.¹³

Developmental defects in the tubular portions of the bovine reproductive tract—Most of these defects are probably hereditary in origin although some cases may be congenital. **Segmental aplasia of the Mullerian or paramesonephric ducts** and especially an **imperforate hymen** have been called “white heifer disease” because of the association of these genetic defects with white coat color. Reviews of these conditions reported that the Mullerian ducts fuse and develop in the bovine embryo when it is 5 to 15 cm. long or is 35 to 120 days of age.^{19,69} The author has grouped these conditions together because the defects as described in England, in Minnesota, and in New York State are very similar.^{2,14,65} “White heifer disease” was so named because it occurs most commonly in white heifers of the Shorthorn breed. This condition is considered to be caused by a single, recessive, sex-limited gene with linkage to the gene for white color.⁶⁵ Besides occurring commonly in about 10 percent of white Shorthorns, it has also been described in roan and red Shorthorns, Angus, Holsteins, Jerseys, Guernseys, Ayrshires and other breeds of cattle. The condition called arrested development of the Mullerian ducts occurred in a Holstein herd due to inbreeding a valuable sire upon his own daughters.¹⁴ Of 23 female offspring that were raised to breeding age, 12, or 56 percent, were sterile and 10 were of either low fertility or normal fertility. On the basis of this report, the condition was definitely due to a single, autosomal, recessive gene causing a sex-linked sterility due to inbreeding to a sire homozygous for this gene.²⁰

No single lesion is descriptive of this condition and a wide variety of anatomical defects may be noted. (See Figures 120–128.) For ease of description the author will generally follow Spriggs’ classification.⁶⁵ Segmental aplasia of uterine tubes is very rare. Two cases were reported in 2230 organs examined in Sweden.⁵⁸ The author has only observed two cases in his entire experience. Rarely a parovarian cyst may obstruct an oviduct.

The most severely affected cattle with segmental aplasia of the paramesonephric ducts are sterile due to the bilateral nature of the defects. These may be characterized by a hymenal constriction; absence of either the cranial part of the vagina, the cervix, or the uterine body, including part of the horns; and a cystic dilation of the uterine horns due to a narrow band of aplasia or a defect near the uterine body. (See Figure 128.) More commonly just the apices of the uterine horns containing yellow, tan to dark-reddish-brown mucus are present. This cystic apical dilation may vary from the size of an acorn to the approximate size of a 4-month pregnant uterus, containing a few ml. to a gallon or more of watery, thick, gummy or inspissated mucus. (See Figures 126, 127.)

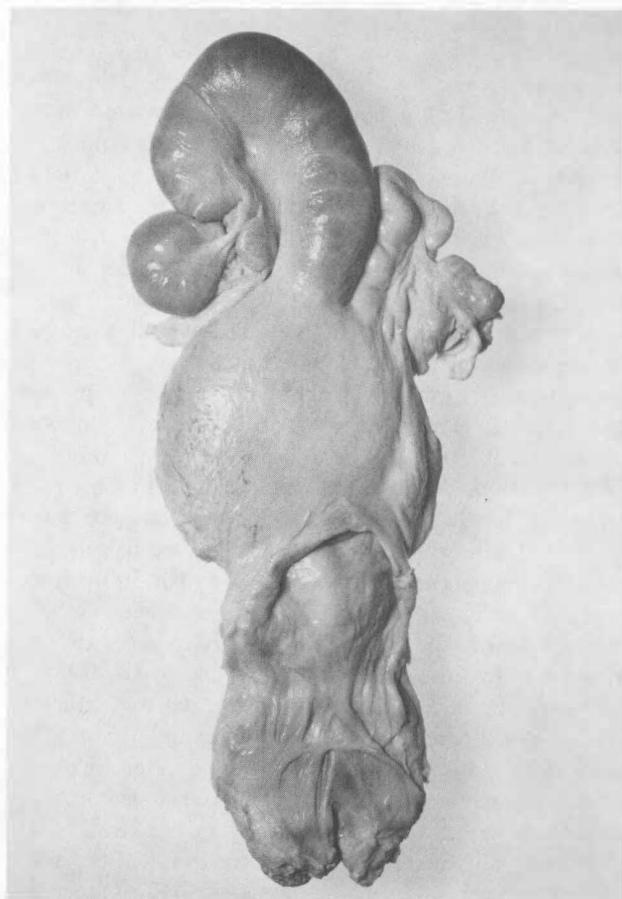


Figure 120. Uterus Didelphys with Unilateral Mucocervix and Mucometra (Note the distention of the left uterine horn simulating a 50-day pregnancy and a CL in the right ovary.)

The cystic apices of the uterine horns may be oval, spherical, or nearly the shape of a normal horn, but they are thin-walled and are likely to be sacculated. In rare cases a cystic sacculcation of the Mullerian duct filled with mucus may develop in the region of the cervix (see Figure 120). These cystic dilations may be unilateral and of unequal sizes, depending on the extent of the aplasia. These above conditions as well as alternate constrictions and dilations of the uterine horns are called segmental aplasia of the Mullerian or paramesonephric ducts.

In rare cases 2 small, parallel, firm tubules or cords with a diameter of 1 to 2 cm. are present in the region of the missing vagina, cervix, and uterus for a distance of 10 to 25 cm. They are usually between the cranial portion of the vagina and the uterine horns or vestiges of the uterine horns. These tubules may fuse to form a rudimentary cervix but usually it is imperfectly formed

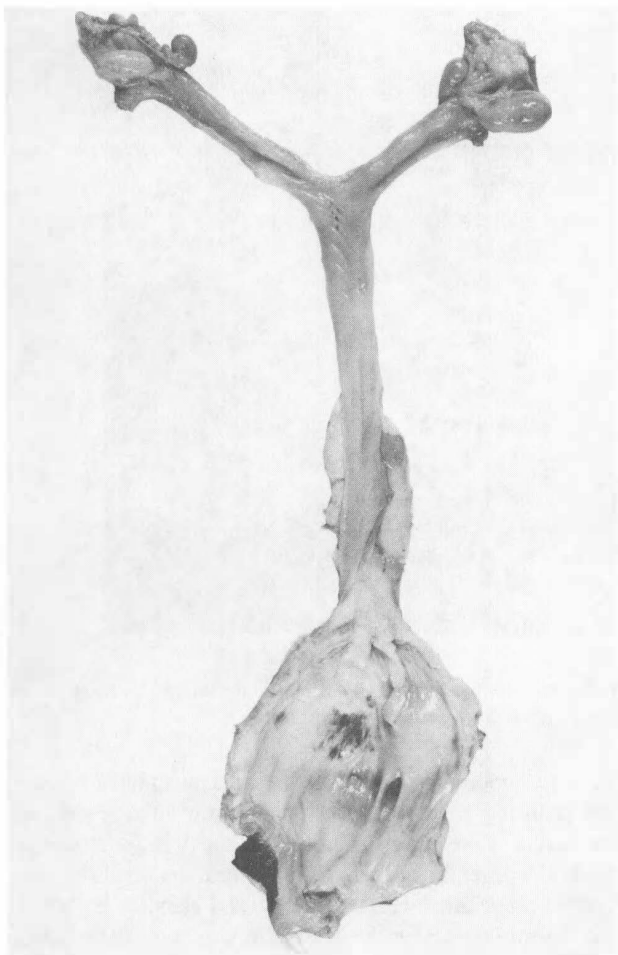


Figure 121. White Heifer Disease With a Marked Aplasia of the Vagina, Cervix and Uterus (Note the normal ovaries, oviducts and vulva).

or even absent. The vagina is usually short and narrow, or may have an enlarged or dilated caudal portion containing mucus or occasionally pus, and submucous vaginal channels may be present. These cordlike structures are considered to be primitive vestiges of arrested development of the Mullerian ducts.^{2,14,70} They might be vestiges of the primitive Wolffian ducts.⁶⁵ Further embryological studies of this condition may be necessary to establish the correct diagnosis and terminology. In rare instances there is a marked arrest in development, aplasia, or hypoplasia of the vagina and Mullerian duct system, characterized by a lack of a normal vagina, cervix, or uterus (see Figure 121).

Segmental aplasia involving the uterine horns is not uncommon and if only one horn is involved, the condition is called a uterus unicornis. (See Figures 125 and 126.) A hymenal constriction may be but usually is not

present. These animals may be fertile or infertile, usually the latter, with prolonged intervals between estrous periods and repeated services per conception because conception cannot occur if ovulation takes place on the side of the abnormal horn and normal involution of the C.L. may not occur due a prostaglandin deficiency caused by the missing uterine horn. In a total of 20 cases of uterus unicornis there were 14 with a normal left horn and a missing or defective right horn, and 6 had a normal right horn with a defective left horn.^{5,14,33,52,65,71} Twenty-six cases of uterus unicornis of which 17 were sterile or probably sterile were reported.⁶⁷ The hereditary nature of these defects of the tubular portion of the bovine genital tract and the danger of their spread by AI bulls was noted. A complete literature review on uterus unicornis was published.²³ The size of the cystic apex of the missing horn varies from 1 to 15 to 20 cm. in diameter. The rest of the anomalous horn is usually a dense, flat band of tissue. In 2 of these cases of uterus unicornis observed by the author the cervix was large and thick and filled with masses of dense mucus, like a cervical seal. In 5 cases the mucus in the cystic apex or incomplete, defective horn had become dried and appeared tan to brown in color, putty-like, gummy, or dried like a dense gum eraser into 2 to 7 irregular-shaped, 1 to 2.5 cm solid masses, with fluid mucus like heavy oil around the dried

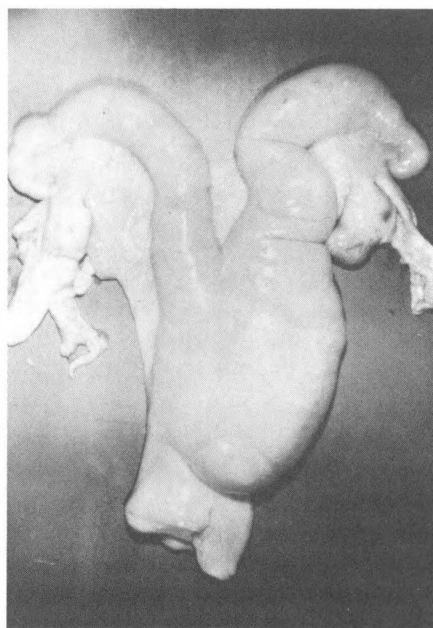


Figure 122. Segmental Aplasia of the Cervix with Secondary Hydrometra in a Heifer. (Note resemblance to a 2-month pregnancy.) (Courtesy K. McEntee.)

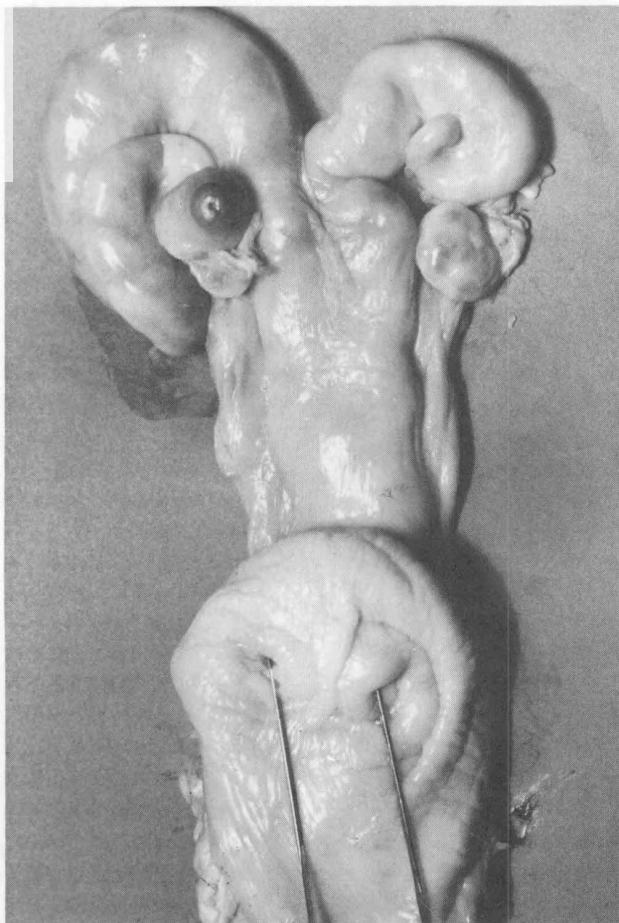


Figure 123. Double External Os of the Cervix Due to the Persistence of the Median Wall of the Paramesonephric Ducts in a Cow. (Courtesy Ohio State Univ.)

or inspissated masses. These objects were composed of cellular and amorphous material. In most cases the mucus was fluid, watery in consistency and a translucent to opaque, yellow to reddish-brown color (see Figure 126).

Congenital lack of endometrial glands in the bovine uterus has been observed in a few heifers. (See section on anestrus.) These heifers exhibited a failure of estrus and a retained or persistent corpus luteum apparently due to a failure of the endometrium to produce the luteolytic factor or prostaglandin necessary for the involution of the corpus luteum. Manual removal of the corpus luteum results in estrus in about 3 to 4 days but the next corpus luteum also persists. The author has observed other sterile heifers that cycled normally but lacked caruncles or caruncular areas in the endometrium. Whether this is genetic or congenital is not known.

Genetic or congenital anomalies of the cervix of cat-

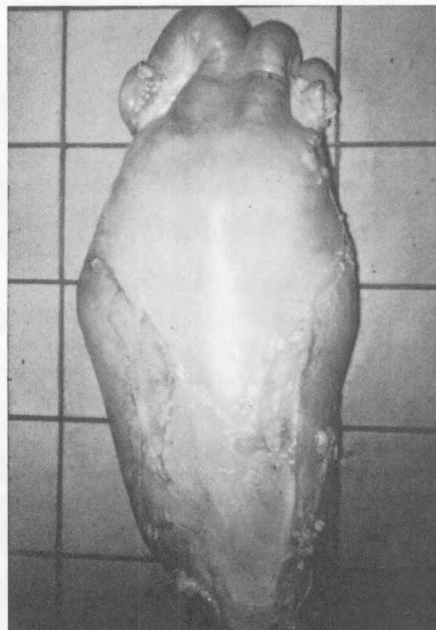


Figure 124. White Heifer Disease with an Imperforate Hymen Causing Mucovagina, Mucocervix and Mucometra.

tle is not uncommon. Segmental aplasia may rarely occur resulting in mucometra or a cystic enlargement of the cervix. (See Figure 120 and 128.) A high incidence of developmental defects of the paramesonephric duct system associated with infertility and sterility in Jersey and Shorthorn heifers in Australia was described.⁵⁰ Besides segmental uterine aplasia infertile heifers had sacculations 1 to 4 cm. in diameter, diverticulums 1 to 2 cm. deep, and dilations of the cervix due to defects at the third or fourth cervical rings. Similar defects have

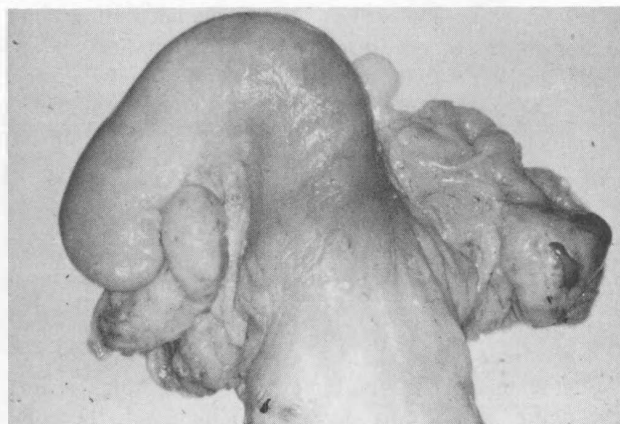


Figure 125. Uterus Unicornis in a Cow.

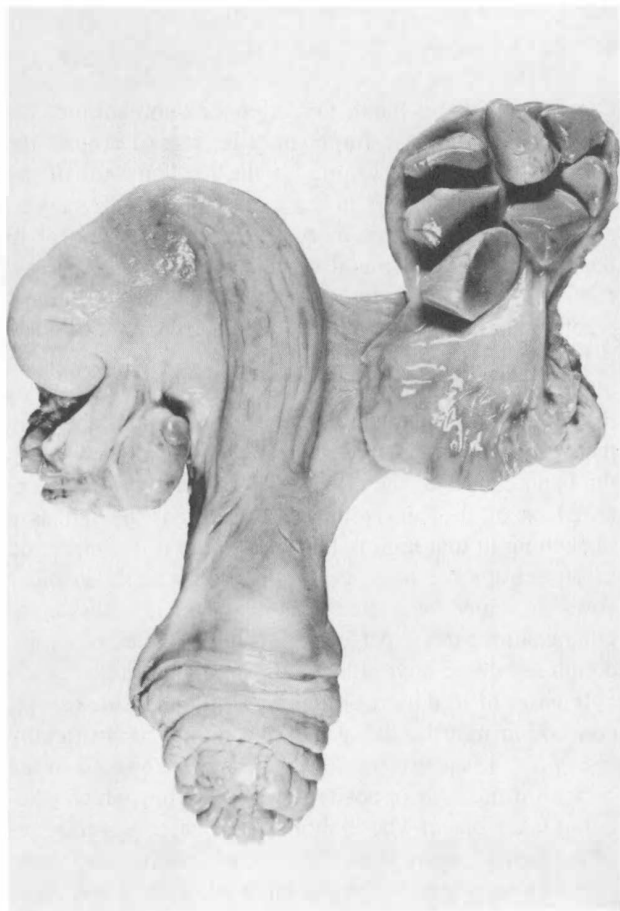


Figure 126. Uterus Unicornis with a Cystic Apex Containing Bodies of Inspissated Mucus.

been observed in Jersey heifers and in other breeds in New York State.^{40,41} These defects are invariably filled with thick mucus and most affected heifers fail to conceive. These may often be diagnosed by rectal palpation of the cervix aided by a small metal probe such as a uterine catheter.

Double external os of the cervix in cattle is occasionally observed and is believed to be an instance of failure of the Mullerian ducts to fuse (see Figure 123). These seldom interfere with conception after natural service. The condition was described as being present in 118 cattle of the Swedish Highland breed, 2 percent of 5,940, sent to slaughter.³³ Many references to the condition in England and elsewhere were cited⁶³ stating that it was present in about 0.2 percent of the cattle. Examination of 514 genital tracts from dairy cattle, mainly Holstein, in New York State in 1969–70 revealed 12 cases or 2.3 percent with a double cervix; in nearly all

cases only the caudal half of the cervix was involved.⁵⁹ It is observed in many breeds, such as Shorthorns, British Friesian, Guernseys, Herefords, Holstein, and Brown Swiss. The condition is normally present in the 7.5-cm.-long bovine fetus but disappears during later fetal life.⁴⁵ There is evidence to show that this condition is hereditary and may be transmitted as a recessive gene. In an extensive review of the double cervix condition in cattle, the incidence varied from 0.1 to 18.2 percent with an average of 0.3 to 7 percent.⁶⁹ The condition was considered to be due to a dominant gene with incomplete penetrance transmitted by either or both the sire and the dam. This condition in Herefords was caused by a single

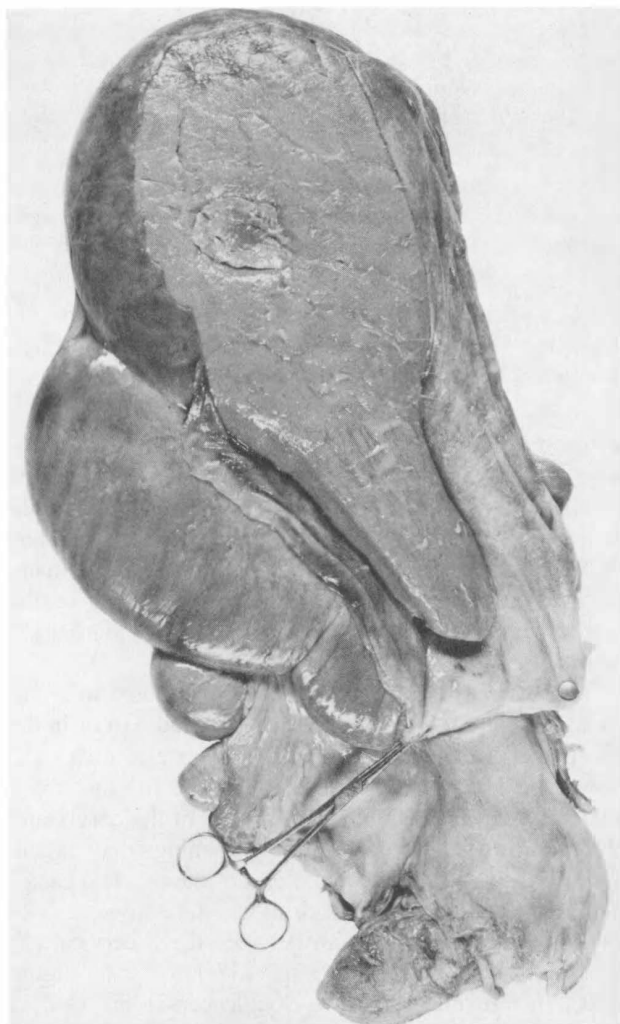


Figure 127. Segmental Aplasia of the Right Uterine Horn Resulting in an Accumulation of Inspissated Mucus. (Note the 90-day-pregnancy in the left horn. The right horn contents resemble a mummified fetus.)

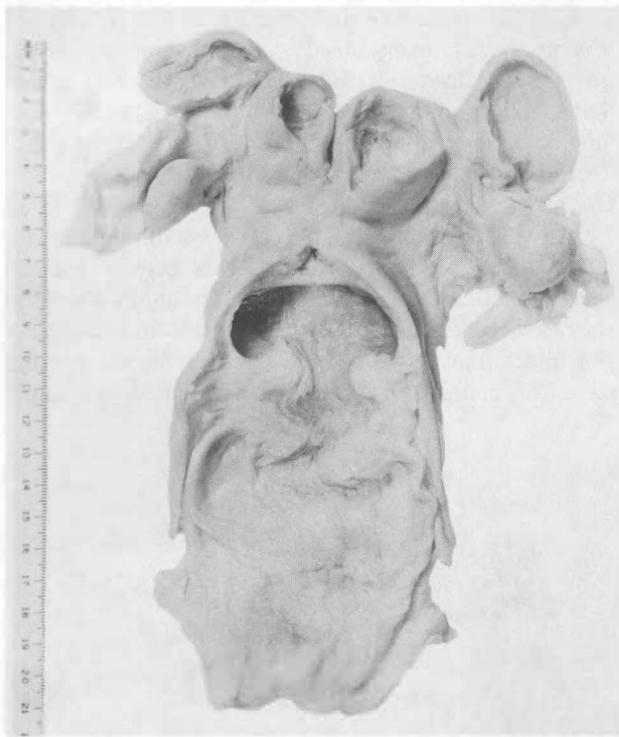


Figure 128. Segmental Aplasia of Both Uterine Horns and Cervix in a Heifer.

autosomal recessive gene with low penetrance and variable expressivity.^{60,61} Most cases are apparently isolated or sporadic and are usually found on clinical examination for sterility or at the time of parturition or slaughter. A bull was reported that sired 18 heifers requiring many services before even 7 became pregnant. Many of the sterile heifers had double cervixes and other genital abnormalities.⁷

The lesion often occurs as a band of tissue 1 to 5 cm. in width and 1 to 2.5 cm in thickness caudal to or in the external os of the cervix. On speculum examination it may appear as if there were a double os. In other cases there may be a true double external os of the cervix and the band of tissue separating the 2 openings may extend for a short way into the caudal part of the cervical canal. Rarely a true double cervix or uterus didelphys may occur with a complete septum between the 2 cervical canals, each opening into its respective horn. (See Figure 120.) In rare instances in a double cervix the median septum between the 2 cervical canals may extend caudally for 4 to 6 inches, producing a doubling of the cranial portion of the vagina or a partially septate vagina.

Affected cows usually conceive and calve normally. Rarely a portion of the fetus will pass on either side of

this band of tissue and result in dystocia that is easily relieved by incising the band. Only slight bleeding will occur. Occasionally the placenta on expulsion may be caught around this band. On vaginal examination of the nonpregnant cow the finger may be passed around the band in the anterior vagina. If the median wall of the Mullerian duct persists in the caudal part of the cervix, a true double cervix or uterus didelphys will appear to be present. Passing metal catheters, probes, or narrow forceps, simultaneously into each external os will reveal whether there is a caudal band in the cervix or a true double cervix. (See Figure 123.) Rectal examination in a case of true double cervix or uterus didelphys reveals the cervix to be characteristically broader and flatter than the normal cervix. On rectal examination of cows with the band caudal to the cervix or the doubling of the external os of the cervix this structure may be felt as a thickening in that region; but more often it is considered as an ectopic or large cervical os, especially in older cows. In many cases diagnosis is not made unless a vaginal examination is performed. Many affected cows undoubtedly never have this condition diagnosed.

In cases of true uterus didelphys with a double cervix, conception may be delayed if the animal is artificially inseminated because the semen may be deposited in the cervix on the side opposite the ovary from which ovulation takes place. The author has observed several "repeat-breeder" cows with this type of uterus. Since only one horn takes part in the placentation of the fetus, abortions, premature births, retained placenta, and infertility are more common in these cows than in animals with a normal uterus and cervix. The cattle with the more extreme aberrations of development should be culled as soon as the condition is diagnosed. The offspring should not be used as breeders without recognizing that the condition is probably hereditary. The lesser abnormalities such as a band caudal to the cervix and possibly a median band in the caudal part of the cervix may be easily removed by surgery. If the band in the cervix is large and extends deep into the cervical canal it should be allowed to remain as it seldom interferes with conception or parturition.

Other anomalies of the bovine cervix may include: a short cervix with one or more transverse rings missing; a lack of development of the cervical rings; and as many as one to three percent of heifers may have a tortuous, a sharply-curved cervix or a hypertrophied transverse cervical ring so that an artificial insemination pipette may not be able to be passed.^{7,40,41} In heifers with a short or underdeveloped cervix, infertility is often due to an endometritis; while the bent, tortuous or stenotic cervix often is filled with thick mucus and infertility may be asso-

ciated with the inability of large numbers of spermatozoa to traverse the cervical canal.

In Brahman, Santa Gertrudis cattle or crossbred Brahman cattle, Beefmaster and Brangus, a marked hypertrophy of the cervix, probably genetic in origin, may commonly be noted especially in pluriparous cows. The cervix may be 10 to 15 cm. in diameter and 15 to 20 cm. or more in length and weigh up to 25 pounds at calving. This may be mistaken for a large mummified fetus on rectal examination. Because of its large size and weight the cervix pulls the vagina forward and downward, occasionally resulting in pneumovagina and a filling of the vagina with urine.^{46,71b} The cause of this hypertrophy is not known but infertility is often present in affected cattle, especially those bred artificially if intra-uterine insemination is not accomplished. Dystocia does not occur due to this hypertrophied cervix but pre- and postpartum cervicovaginal prolapse is common.^{71b} This infertility may be due to delayed involution of the pendent cervix and uterus, the difficulty of fixing the cervix with the rectal hand and passing the insemination pipette through the hypertrophied transverse rings; or be due to the lowered number of spermatozoa able to traverse the greatly hypertrophied cervix since these cows are fertile if bred naturally. The uterus is normal in size. An increase in the size of the cervix is progressive during pregnancy. Cows with hypertrophic cervixes are often culled in herds in which AI or embryo transfers (non-surgical) are performed. Herd managers and veterinarians have a definite impression that selection against bulls with large pendulous sheaths may also reduce the incidence of hyperophied cervixes in a herd.^{71b} Further study on this condition is indicated.

Infertile heifers with a double cervix, tortuous or kinked cervix or a cervix with a dilation or sacculum probably should be culled because of the possible genetic nature of the defect. However these heifers may conceive on repeated natural or artificial service even though in the latter instance the insemination pipette cannot be passed to the cranial portion of the cervix for the deposition of the semen. Careful expert manipulation of the AI pipette or the use of a metal uterine catheter of small diameter, such as the Luken's, or Woelffer catheters, may enable the operator to deposit the semen properly. These techniques are also indicated in the heifers of small breeds such as the Angus and Jersey with a normal but small, possibly juvenile cervix. The incidence of these latter cases with constriction of the cervix was reported to be about 0.1 percent.⁴⁴ In an attempt to overcome this constriction in certain heifers, some veterinarians have injected several doses of estrogens at intervals of several weeks to cause a greater growth or maturity in the gen-

ital tract and a larger cervix and cervical canal.

In most cases described above the cervical canal is not completely occluded otherwise mucometra would develop due to the inability of mucus to escape from the uterus. In rare cases when natural service and attempts at artificial insemination fail to result in conception in cattle with cervical defects, diluted or preferably undiluted semen may be injected by means of a long needle through the rectal wall, vaginal wall or ischiorectal fossa into the uterine lumen or into the region of the ovary and fimbria of the oviduct on the side of the ovary with the mature Graafian follicle.^{12,27,39,62} A small amount of air should precede the injection of semen into the uterine lumen to make certain of the location of the tip of the needle. Four of 6 heifers that had been bred repeatedly and had a tortuous, twisted cervix conceived on first service and calved normally when the semen was injected intraperitoneally adjacent to the ovarian follicle.²⁷ The prognosis for conception by this procedure to bypass a defective cervix is guarded and is probably seldom indicated or desirable.

Developmental defects of the vagina are largely limited to the partially persistent or imperforate hymen, unusual cases of obliteration of the caudal portion of the vagina,⁴⁷ and, as previously described, persistence of the median wall of the paramesonephric duct in the cranial portion of the vagina most commonly seen as a fleshy band just caudal to the external os of the cervix or as a median septum extending 3 to 6 inches caudally resulting in a septate vagina associated with a double cervix. These defects are also probably hereditary in nature although a few may be congenital. (See Figures 121, 123, 124.)

Thin fenestrated hymenal membranes or dorsal ventral bands in the region of the vestibular-vaginal border are fairly common in young heifers but are of no significance as they do not obstruct the genital passage and are easily broken at coitus.^{40,41} In cases where the hymen is imperforate the condition is also called "white heifer disease." This condition may be associated with segmental defects of the paramesonephric ducts. In one Shorthorn herd, 9 of 23 white heifers, 4 of 115 roan heifers and 1 of 94 red heifers were affected.⁵¹ The genital tract of all white Shorthorn heifer calves should be examined in a manner similar to a technique used for diagnosing freemartin calves. Shorthorn bulls known to be carriers of the gene for imperforate hymen or segmental aplasia should be bred only to dark roan or red females.^{64,65} The condition of an imperforate hymen may also be seen in Holsteins, Ayrshires, and other breeds of cattle. In these affected cattle the rest of the genital tract is often normal. The animals show regular estrous cycles and symp-

toms of estrum. The genital tract fills with mucus that is usually amber to dark reddish-brown in color due to metestrual bleeding and may vary in amount from several quarts to 2 or more gallons. Service by artificial insemination is impossible and normal or physiologic coitus by the bull is frequently followed by slight hemorrhage and straining or tenesmus. In rare cases rupture of the vaginal wall during natural service may occur with a secondary perivaginal abscess. Rupture of the hymen and a secondary pyometra may develop due to the introduction of infection into the genital tract without proper drainage being possible. If the vaginal distention becomes great, straining may result after service or even before puberty, and the distended, bulging hymen may show between the vulvar lips with each abdominal contraction or when the heifer lies down. Frequent urination may accompany the tenesmus. In areas in which rabies is endemic this disease may be confused with tenesmus seen in many rabid cattle. In a yearling Holstein heifer observed by the author the greatly distended vagina, containing about 3 to 4 gallons of mucus, caused pressure necrosis and rupture of the bladder, and death of the heifer due to peritonitis and uremia. (See Figure 124.) Another case was observed in a 7-month-old Shorthorn heifer in which an ulcer and perforation of the distended uterine horn occurred followed by peritonitis and death. In these heifers the cervix is usually somewhat dilated and the uterine horns are distended similar to a pregnancy of 60 days or more. Horns or portions of horns distended with mucus in segmental aplasia of the paramesonephric ducts may also lead to a mistaken diagnosis of pregnancy. If conception does occur with heifers having a nearly complete hymen, in some cases a dystocia may result at the time of parturition that will be relieved only by deep episiotomy incisions of the dorsolateral and lateral walls of the vulva. Bleeding may be severe. The prognosis in cases of imperforate hymen is guarded to poor.^{64,65} The author operated upon one heifer and the animal calved three times subsequently. Other veterinarians have reported similar results.

In affected heifers following the administration of epidural anesthesia the imperforate hymen may be incised over the point of the greatest bulge allowing the mucus to escape. The incision should then be carefully enlarged at right angles in 4 directions. Some veterinarians advise removing the imperforate hymen by a circular incision completely around the margin of the vulvovaginal border. If the heifer is to be kept for some time before slaughter, or if breeding is to be attempted, the vulvovaginal ring should be dilated with a speculum every 2 to 3 days for 2 weeks. Care and attention should be paid to cleanliness, to prevent the introduction of infection

resulting in pyometra or metritis. If the vestibulo-vaginal border is very small and stenosed the prognosis is poor and the animal should not be bred lest severe dystocia result at parturition. Two cases of imperforate hymen were reported that apparently healed following service by a bull.¹⁶ At the time of calving dystocia resulted requiring incising of the thickened hymen. The author observed an imperforate hymen in a Guernsey heifer that had been "inseminated" artificially on several occasions by a lay technician. The pipette had apparently been introduced through the urethra and into the bladder causing a severe pyelonephritis.

Twelve daughters of one Holstein bull that had various defects of the genital tract causing sterility was described. In 10 of these heifers the AI pipette could only be inserted 6 or 7 cm. or the length of the vestibule and the anterior portion of the vagina was distended up to 8 inches in diameter with mucus.⁴⁷ In these cases there was an obliteration of the caudal portion of the vagina, due to an incomplete recanalization of the vaginal anlage in the embryo, not just a simple imperforate hymenal membrane. About half of these cases also had a uterus unicornis.

Abnormal Wolffian or Gartner's Ducts—Abnormalities of Gartner's ducts which are vestiges of the primitive Wolffian or mesonephric ducts in the embryo are rather common in the cow (See Figure 129). It is not known whether these defects are hereditary. In hyperkeratosis due to chlorinated naphthalene poisoning the Gartner's ducts become greatly enlarged due to metaplastic changes in the epithelial linings of the ducts.⁴² Normally these ducts are located beneath the mucosa of the floor of the vagina. They are 2 in number and are usually difficult to detect. The duct may develop multiple cysts along its course toward the cervix or form a long, sometimes rather coiled, cord 0.5 to 1.5 cm. in diameter distended with fluid. In rare instances infection of the duct may occur, with small abscesses forming along its course. In one case calculi were found.⁷⁰ The ducts may be incised freely, if necessary, to correct these abnormalities but in most cases they are ignored as they do not affect fertility. There may be present in rare cases a cul-de-sac extending forward 5 to 7 cm on either side of the urethral opening.⁷⁰ This may be small and admit one finger or less; or it may be large admitting 3 to 4 fingers. This cul-de-sac represents an abnormally large terminus of Gartner's duct and may interfere with coitus.

Rectovaginal Constriction (RVC), Anovestibular Stenosis or an infantile, hypoplastic, small vulva was described in 1940 affecting the daughters of one Jersey bull. In 7 daughters the vulva was so small that at parturition a drastic episiotomy operation was required to

enlarge it so that the fetus could be removed. In one case cesarean section was necessary. Recently this condition has been carefully described as a simple autosomal recessive defect of Jersey cattle resulting in a severe stenosis or constriction of the anus and vestibule. Copulation and defecation can occur but rectal examinations in both bulls and cows and parturition in cows cannot occur and severe dystocia results.^{36b,c,43a} The strong band of connective tissue causing the stenosis or constriction encircles both the anus and vestibule.

Miscellaneous Hereditary Forms of Infertility in Cows

Freemartins, or sterile heifers born cotwin to a bull, occur in about 90 percent of the bovine twin births of opposite sexes. Twinning has been discussed and shown previously to be greatly influenced by heredity. This was reviewed and the hereditary aspects of this problem in cattle are fairly well understood (See Freemartinism).¹⁸

Cytogenetics in cattle and the inheritance of related defects has been reviewed.^{11,22} Fairly extensive studies have been conducted on freemartinism and the 1/29 Robertsonian or centric fusion translocation. A few XO and XXX female cattle have been described.^{11,37} Small ovaries and anestrus were observed in several of these heifers. The 1/29 translocation, which is believed to be an ancient mutation, is widely distributed in about 30 European breeds, especially the beef breeds of cattle. The incidence in these breeds varies from 0.5 to 20 percent.²² It has been reported in the U.S.A. The reduced fertility of heterozygous bulls and cows is well-established. Elimination of heterozygous A.I. bulls raised the

fertility rates in cattle bred artificially. Although not proven there is apparently a 3 to 4.5 percent embryonic death loss between 30 and 90 days of gestation in cows bred to heterozygous bulls.²² Cattle populations using artificial insemination should conduct routine cytogenetic investigations of their donor bulls. It would be desirable to conduct widespread cytogenetic surveys in cattle as has been done in humans in which more than 50 percent of spontaneous early abortions of human embryos are chromosomally aberrant.¹¹ About 5 of 1000 liveborn babies have chromosomal defects.

Intersexes or hermaphrodites are observed occasionally in cattle. There are no reports on cattle that this condition is due to heredity, as in goats, swine and possibly sheep.

Nymphomania or cystic ovaries is influenced by hereditary factors, as indicated previously. This hereditary predisposition toward cystic ovaries is closely associated with high levels of milk production but not to total fat or fat percentage. The relationship was a physiological-hormonal one and that genetic correlation between high milk yield and cystic ovaries had not been proved. Cystic ovaries are more frequent in daughters of cows having cystic ovaries and in daughters of certain bulls. (See Cystic Ovaries.)

Jersey and Holstein female sterility observed in heifers was reported.^{20,21,29} This data indicated that random inbreeding of selected sires and dams showed they carried autosomal recessive genes for female sterility as based on failures of heifers to conceive. The Jerseys showed regular estrous cycles whereas the Holsteins exhibited irregular estrous periods and usually anestrus. It is unfortunate that careful anatomical, histological, and bacteriological examinations of the genital tracts, ovaries, and pituitaries of these sterile heifers were not performed.

In Sweden the percent of heifers pregnant on first insemination is 6 percent higher in the SKB or Highland breed, despite the problem of gonadal hypoplasia, than the SRB breed. These breed differences are genetically conditioned.¹ In the U.S.A. the Guernsey breed is generally considered to have lower fertility than the Holstein or Jersey breeds based on nonreturn rates to artificial insemination. The pregnancy rate in over 10,000 beef cows was studied over a 5-year period. The pregnancy rate for Zebu purebreds or crosses, Brahman or Santa Gertrudis were definitely lower than the British breeds, Hereford and Angus, 57 vs 72.5 percent. Further study is desirable and needed.⁴³

Sexual behavior in the cow has been shown to be affected by heredity.⁷² The estrous cycles in an individual cow tend to be of similar length. Variations in cycle length were much more common between cows than



Figure 129. Cystic Gartner's or Mesonephric Ducts in the Floor of the Vagina. (Courtesy K. McEntee.)

within individual cows. When normal cycles of 18 to 24 days are considered there is a great tendency in each cow to maintain a consistent cycle length. In individual cows there was a definite tendency of the interval between parturition and the first estrus to remain similar after each parturition.^{48,49} Daughters had similar records to their dams, and daughters by the same bull also tended to be similar. The heritability for the time at which estrus occurs after calving was about 30 percent.

"Weak" symptoms of estrus were one of the most common or troublesome problems in artificial insemination. These "weak" or nearly "silent" estrous periods were observed most commonly in certain breeds of cattle such as the Swedish Red Cattle, while other breeds such as the Simenthaler, Telmark, and Swedish Highland cattle exhibited intense symptoms of estrus even in an unfavorable environment.^{30,32} The genetic difference in potency and strength of signs of estrus between dairy, beef and other breeds was noted.⁵³ This difference between breeds has not been as noticeable in the United States. It has been observed by the author as occurring in certain families of Guernsey and Holstein cattle, most commonly in the former breed. Repeat breeding is more common in cows with a weak estrus because of the difficulty of timing artificial insemination in relation to ovulation. When 34,063 cows with "weak" heat signs, as determined by the inseminator and the herdsman, were compared with 263,906 cows with normal heat signs and inseminations were made early, intermediate or late in the estrous period, the percent pregnant were 39.5, 45.6 and 50.2 and 55.3, 57.9 and 55.1, respectively. Thus cows with "weak" heats had a 10 percent lower pregnancy rate possibly due to delayed ovulation since the least difference occurred in the cows bred late in the estrous period.¹ A study of 29 bulls used artificially with regard to the heat symptoms in their daughters showed this trait to be partially hereditary.⁵⁴ Cows conceiving on first service had stronger heat signs than those cows failing to conceive.

Inbreeding and fertility—Several references were cited to show that inbreeding generally may result in reduced fertility, but that the degree of the infertility depends on the particular bull used. The effect of inbreeding on fertility is uniquely the property of a particular line or family.²⁸ Inbred lines of cattle usually experience reproductive trouble but if the line is not eliminated by its deleterious genes, as often happens, then fertility may remain fairly satisfactory. Inbreeding of the zygote and dam, and homozygosity for blood group factors greatly increased embryonic mortality.^{3,38} Lower conception rates occurred when the potential embryo was inbred rather than outbred and pregnancy loss was greater when the

dam was inbred rather than outbred. Heterosis improved fertility.

Production and fertility. On the basis of relatively small numbers, high-producing cows were no more often disposed of as infertile than were low-producing cows.⁷² The relationship between high-butter-fat yield and ovarian hypoplasia and high milk yield and cystic ovaries has previously been mentioned. Probably more study on this phase of fertility from the hereditary aspect is indicated but at present most data indicates that milk production is not associated with infertility.

The inheritance of normal fertility or lowered fertility may be studied from a number of aspects, including inheritance from bulls to their daughters, from dams to their daughters, from bulls to bulls, and from dams to bulls. Only the first 2 aspects have been studied. It has been noted that workers in estimating fertility have difficulty in obtaining a standard or means of measuring fertility.^{15,72} This was not a problem when specific genes were involved as in ovarian hypoplasia and segmental aplasia of the Mullerian ducts, but it is a great problem when measuring reduced or subfertility. The conception rate is a good measure but does not take into consideration those animals that fail to show regular estrus. It excludes barren heifers or cows, if figures are obtained from calving dates. If the figures include animals that abort, the results may be biased because some less-valuable animals may be sold as sterile after several breedings while more valuable animals may be retained and eventually conceive. Calving intervals may be used to measure fertility but they include only animals that have calved, and may be biased by a planned extension of calving intervals in cases of persistent or heavy producers. Completely sterile animals may be studied separately but this excludes the large group exhibiting reduced fertility. For these reasons most studies on infertility are not comprehensive. Some investigations using certain indices show that genetic factors are unimportant, but nearly all can be questioned on the basis of bias in the material. Similarly many investigations show genetic factors to be important but these can usually be criticized because they deal with only one breed or herd or family and one particular character. Thus care should be taken to avoid generalizations on the basis of only a few studies. Possibly the problems of inheritance of fertility in cattle cannot be arrived at until the problem of disease has been adequately controlled.

Research on the relative fertility of the daughters of different bulls has been summarized.^{4,18,48,49,53,68,72} There appeared to be a difference in the fertility of daughters of various bulls. Other studies showed that on the basis of nonreturns to first service and calving intervals the

difference in fertility between daughters of various sires was small.⁶ Thus preference in breeding should be given to those sires whose daughters were of high fertility. However, some inbreeding studies and studies in which certain sires transmitted a specific defect must be considered. Sex-linked genes for infertility in daughters of certain bulls was reported.^{20,29}

The inheritance of fertility from female to female, as shown by many workers has been studied from the standpoint of the recurrence of any given pattern of breeding ability.^{15,18,53,72} Most workers have concluded that the condition of "repeat-breeding" is not very permanent.^{48,49,68} However, there is a slight tendency to repeat the same breeding pattern from one service period to the next. In studying cow families, considerable differences in reproductive efficiency as measured by calving intervals and conception rates were reported.⁶⁸ Other workers reported little difference between cow families and noted that cows in cow families are not as a rule closely related.⁷² Thus in respect to cow families the inheritance of infertility based on a number of studies is contradictory and unpredictable. In studying **dam-daughter comparisons** the heritability of conception rate is not high and is probably under 10 percent.⁷² **Herd differences in fertility**, even though genetic composition varied greatly, were affected little or not at all by genetic differences.^{48,49,68,72} Since the genetic composition of a herd does not vary much from year to year and fertility may vary markedly, it is rather obvious that most of the herd differences in fertility are due to environmental rather than to genetic causes.

From the above studies about 80 percent of the variation in normal fertility in herds is due to environmental causes and that of the remaining 20 percent about one-half would appear to be due to various additive genetic effects.⁷² Selection for fertility cannot be very effective.^{6,8,15} Automatic natural selection against infertility is going on constantly. It is possible that epistatic effects are responsible for much of the permanent differences between cows. If this is true, cross breeding to produce heterosis is a better genetic method than is selection for improving fertility.⁷² It may be true that specific breeds adapted to certain environments would be necessary to obtain maximum fertility. In either case environmental influences would still make genetic progress very slow. Little attention need be paid to selective breeding as an effective means of raising fertility but should be considered constantly when advising farmers on aspects of inbreeding or on definite evidences of a single gene predisposing to or causing sterility. There is a great natural prolificacy in the dairy breeds.⁷² In the Dexter breed, despite the death of 25 percent of the bulldog fetuses,

and a ban on breeding another 25 percent of the Kerry type heifers, the breed can still continue to expand a little. It was concluded that although sterility is economically costly it would have to be very severe to cause a reduction in a breed or herd due to lack of replacements.

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Other Pathological Causes for Bovine Infertility

The pathological causes of infertility or sterility due to genetic or congenital defects, hormonal disturbances, and venereal infections have been discussed. Most of the following pathological conditions are the result of trauma or infection or both. They are acquired most commonly at or after parturition, producing lesions that may interfere with the future fertility of the cow. Occasionally tumors of the genital organs may be found. The gross abnormalities and pathology of the bovine genital tract have been surveyed and reviewed by various authors studying clinical findings and slaughter house material.^{10,40,42,46,56a,64,72,77,86,94} These authors attempted to evaluate their findings with regard to infertility, sterility and repeat breeding.

Ovary

Most of the ovarian pathology has been previously considered under the endocrine and hereditary abnormalities of the reproductive tract. However; a few conditions remain to be described.

Ovarian Tumors in the cow have been described fairly often but they are uncommon in occurrence.^{54,67a} Two malignant tumors of the ovary of the cow, an angiosarcoma and a carcinoma were reported.⁹² A fibroma of cow's ovary was described.²² Seven carcinomas of the ovary have been described.^{21,90} In 6,286 bovine genital tracts examined there were 13 ovarian tumors: 3 were carcinomas, 3 granulosa cell tumors, a sarcoma, a fibrosarcoma, and 5 undiagnosed.⁴⁰ In rare cases primary tumors may metastasize to the ovary. Other ovarian tu-

mors include: dysgerminoma, mucinous adenocarcinoma, cystadenoma, arrhenoblastoma, vascular hamartoma, luteoma, dermoid cyst or teratoma containing hair, theca-cell and mixed theca-cell-granulosa cell and lymphosarcoma.^{2,5,11,46,48,54,63,67a,84,88} Thirteen ovarian teratomas were found in 4000 grade Zebu genital tracts recovered from an abattoir. These were cyst-like structures lined with stratified, keratinizing epithelium and respiratory epithelium. The affected ovaries varied in size from slightly enlarged to 75 gms. Seven of the thirteen cows with ovarian teratomas were pregnant.⁴⁵ In cases of cystadenomas, the tumor spread by contact to the peritoneum resulting in ascites.^{5,84} The author reported on two granulosa cell tumors, one in a 15-month-old Guernsey heifer, the other in a 14-year-old Angus cow. He cited references in the literature to 7 other reports on granulosa cell tumor of the bovine ovary⁷³ (see Figure 130). In 3 cases in which the breeding history was known, the animals showed symptoms of chronic nymphomania with frequent prolonged symptoms of estrus and relaxation of the pelvic ligaments. Two of these cases were heifers in which udder development and lactation occurred. A similar case was described in which the cystic fluid in the tumor contained progesterone and estradiol in a ratio of 6:1 parts, respectively.⁸¹ Continuous estrus was explained on the basis of progesterone potentiating the action of the estrogen. An aged Holstein cow exhibited nymphomania, masculinization and anestrus. A 20 lb. granulosa tumor was removed. Cysts on the other ovary occurred but following treatment the cow conceived. Prior to surgery plasma estrogens and testosterone were elevated to 36 to 75 pg/ml and 54 to 130 pg/ml respectively but progesterone levels were low <0.5 ng/ml.⁴ In other cases where the history was known either anestrus or no observable symptoms were noted, and the cows were pregnant or had normal estrous cycles. Granulosa cell tumors may be either solid and yellow in color, or filled with multiple cysts 1 to 7.5 cm in diameter or be composed of a single large cyst. Any cyst larger than a grapefruit, 10 cm., should be suspected of being a granulosa cell tumor. The weight and size of a large ovarian tumor tends to drag the ovary downward and forward into the abdominal cavity. The ovarian artery to large tumors is likely to be increased in diameter. Sometimes it is necessary to place forceps on the cervix and pull the uterus and ovary upward and backward in order to palpate the tumor. Granulosa cell tumors may affect cattle of all ages from calves to old cows.³⁶ Seventeen of 18 bovine ovarian neoplasms studied were granulosa cell tumors.⁴⁸ Granulosa cell tumors were most commonly observed in Guernsey cows. In 4 cases the tumors were found in related animals. In one cow, with a failure of

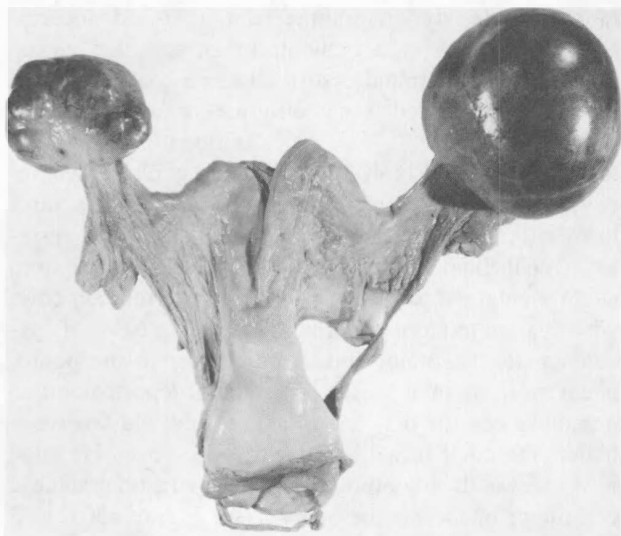


Figure 130. Bilateral Granulosa Cell Tumors of the Ovaries of a Cow. (The tumor on the left ovary is solid and lobulated and on the right the tumor is cystic. The uterine wall is flaccid and atrophied due to prolonged steroid stimulation.)

estrus for 6 months, mucometra developed. Three of the tumors were bilateral and only 1 was malignant (see Figure 130). The size varied from microscopic growths to tumors weighing over 25 lbs. The granulosa cell tumor is the most common one in cattle. It may rarely be malignant and spread to adjacent peritoneal surfaces.^{89b} It is usually unilateral. The earlier reported cases of some of the ovarian carcinomas in the cow may have been granulosa cell tumors. Some of these tumors produce estrogen, as shown by the symptoms of nymphomania, relaxation of pelvic ligaments, and lactation in heifers. In rare cases large cysts containing 1 to 2 or more quarts of fluid may be associated with a granulosa cell tumor of the ovary. In the cases observed by the author and his associates these very large cysts contain fluid with no estrogen content on assay or as shown by physical change in the cow. Cows can conceive with unilateral granulosa cell tumors if little or no steroid hormone is elaborated by the tumor. There are very few reports on the successful removal of these tumors, with the cow conceiving following treatment.

Ovaritis, Inflammation or Infection of the Ovary, may occur secondary to trauma, to infection from the uterus that passes through the uterine tubes, or by extension through the uterine walls causing a peritonitis and perimetritis. Trauma may frequently be produced by rough handling or massage of the ovary. Scars, usually starshaped or transverse, are common in the ovaries of

the cows where corpora lutea have been enucleated or cysts ruptured by manual manipulation per rectum. Bleeding may occur as previously described and a hematoma form around the ovary; subsequently this hematoma organizes and produces extensive adhesions. (See Figure 131.) Inflammation of the ovary or oophoritis will be considered more fully under the discussion of lesions of the uterine tube especially the distal, fimbriated end, or pavilion. Rarely abscessation of the ovary may follow removal of the corpus luteum in cows with pyometra.⁴⁵ Serosal granulomas may be present on the ovary in peritoneal tuberculosis. Particularly in heifers, small tags of fibrin from bleeding after ovulation are frequently observed attached to the ovary at the site of a previous ovulation or on the medial attachment of the ovary to the uteroovarian ligament. These do not interfere with subsequent ovulations or conceptions.

Parovarian cysts are occasionally found in the broad ligament of the cow around the ovary and uterine tube. These cysts are vestiges of the Wolffian or mesonephric duct system or the paramesonephric or Mullerian duct system and may be from 1 to 5 cm. or more in diameter. They are usually round or oval in shape. Most para-



Figure 131. Bilateral Hydrosalpinges with Adhesions Surrounding the Left Ovary of a Sterile Cow.

mesonephric duct cysts are located near or in the fimbria of the uterine tube. Germinal inclusion or "serosal" cysts about 0.2 to 0.5 cm in diameter may rarely be noted on the surface of the ovary. Occasionally the corpus luteum is black in color, **corpus nigrum**. This is apparently of no significance, as these corpora lutea apparently function normally. In rare instances the **tubules of the rete ovarii** may be confused with a neoplastic growth.⁴⁸ The **rete ovarii**, when found in the cow is a network arrangement of medullary tubules found near the mesovarium. Parovarian cysts are less common in the cow than in the bitch, ewe and mare.

Uterine Tube (Oviduct)

Disease of the uterine tubes or Fallopian tubes and ovarian bursae of cattle occurs more commonly than is generally assumed or diagnosed on rectal palpation. Pathology of the ovary and oviduct has been reviewed.⁵⁴ Only abnormalities associated with tubal enlargements and adhesions are detectable on rectal palpation. The incidence of these lesions affecting the uterine tubes should decrease in the future with the use of prostaglandins to cause involution of the corpora lutea rather than manual removal of the corpora lutea.

These many workers and others^{13,14} showed the incidence of disease of the bovine uterine tube and ovarian

bursae to be about 10 percent. Of those 25 percent may be bilateral lesions and interfere with passage of the spermatozoa, with ovulation, and with passage of the ova to the uterus resulting in infertility or sterility. Clinical examinations in over 20,000 cows revealed an incidence of uterine tubal disease of 1.3 percent including 0.2 percent of hydrosalpinx.⁹⁴ (See Table 20.)

The etiological factors causing these lesions are varied. Many lesions are secondary to an ascending infection from the uterus following abortion, retained placenta, septic metritis, and pyometra. Septic metritis with a perimetritis may cause extensive adhesions of the uterine tubes, ovaries, and uterus to the adjacent structures and organs. Abortions, retained placenta, and dystocia with forced extraction frequently lead to salpingo-ovarian-bursal changes.⁶⁷ In certain countries tuberculosis of the uterine tube is not an uncommon cause of lesions.

Anomalies such as segmental aplasia of the paramesonephric duct rarely involve the uterine tube. In rare instances periovarian cysts may obstruct the uterine tube; several cases have been described.^{46,56} (See the previous section on genetic defects of the reproductive tract.) Tumors of the oviduct have not been reported.

Diseases of the uterine tube are more common in the cow than in the mare, possibly because in the latter the uterine tube opens on a muscular papilla in the uterus. In the cow the uterine horns become smaller and blend into the uterine tube. A variety of infectious organisms

Table 20. Incidence of Gross Lesions of the Uterine Tubes in Slaughtered Cattle

References	Number of Cows	Percent Cows with Bilateral Lesions	Total Percent Affected Cows
Carpenter, Williams and Gilman (R) ^{74b}	1221		15.3
Rowson ⁷⁷	296	6.0	13.0
Spriggs (R) ^{74b}	1250	1.3	4.0
Thygesen (R) ^{74b}	1614	2.0	8.8
Lombard, Morgan and McNutt ⁴²	154 ¹	2.0	13.0 ²
Nielsen ⁶⁷	2655 ³	3.1	16.7
McEntee ⁴⁶	240		10.4
Moberg ⁵⁶	1622	4.2	15.5 ⁴
Cembrowicz ¹⁰	300 ⁵		2.0
	730	0.3	8.9
Mylrea ⁶⁴	333	1.8	13.5
Duchateau and Whitmore ¹⁹	250	2.0	5.2
		2.52	10.5

¹Repeat breeders.

²An additional 5.8 percent had microscopic lesions of interstitial salpingitis.

³These were clinical not slaughter cases.

⁴Only 4.8 percent detected by rectal palpation.

⁵These were heifers (nullipara).

⁶Reference in first edition (1956).

may occasionally be found in the infected tube that are similar to those found in the infected uterus; these include streptococci, campylobacter, staphylococci, *E. coli*, *C. pyogenes*, ureaplasmas, mycoplasma, *Hemophilus somnus*, and other ubiquitous "wound" or lower genital tract infections. It is doubtful that coital infections result in salpingitis except possibly as previously described in "epivag," vibriosis, and myco- and ureaplasmosis.^{18a,b,c,41a} Cysts and nodules were found in the oviduct in 87 cases but these apparently were not significant inasmuch as they failed to prevent the passage of the ovum.⁴²

All authors indicated that sterility treatment was a common cause for lesions of the oviduct and bursa. Of these sterility treatments the most common cause of lesions was enucleation of the corpus luteum. The frequency and severity of bleeding due to removal of the corpus luteum has been cited. The majority of the lesions observed were of the descending type due to hemorrhages occurring at ovulation or manual ovarian treatment with removal of the corpus luteum, and the presence of the corpus luteum and hematomas in the bursa or adherent to some of the pelvic organs.⁵⁶ These hematomas organize and produce moderate to extensive adhesions. All serious cases with complete obstruction of the tube resulting in hydrosalpinx were due to extensive hemorrhage. Most authors have noted mild fibrous adhesions between the ovaries and the bursae of heifers



Figure 132. Ovarian Adhesions and Hydrosalpinx in a Cow. (Courtesy K. McEntee.)

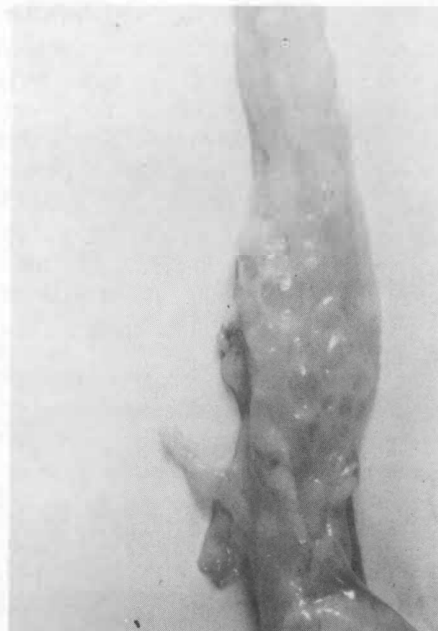


Figure 133. Intramucosal Cysts or Cysts of the Diverticula of the Bovine Uterine Tube. (Courtesy K. McEntee.)

or cows that have never been examined or had an infected uterus. These mild adhesions probably follow the slight bleeding occurring at ovulation. Severe trauma caused by manual rupture of thick-walled follicular cysts, luteal cysts or cystic corpora lutea may result in adhesions, although in the former usually little bleeding occurs. Some authors have reported adhesions following uterine irrigation with or without perforation of the uterus.

The pathologic lesions may vary from a few slight fibrous threads between the bursa and ovary, partial adhesion of the edge of the bursa to the ovary, roughness of the internal wall of the bursa, shallow or narrow or closed bursa, to extensive ovario-bursal lesions, cysts of the bursa or ventricle, hydrosalpinx, and pyosalpinx. The histologic changes in the uterine tube due to chronic salpingitis and other changes have been described.^{42,46} Hydrosalpinx has been observed secondary to anomalies of the reproductive tract, such as segmental aplasia of the paramesonephric duct. It may occur secondary to adhesions of either or both the distal or proximal ends of the uterine tube (See Figure 131 and 132). On postmortem examination if the adhesion is near the distal end of the uterine tube, the mucus in the tube may be pressed into the uterus. The oviduct usually becomes distended to a diameter of 0.5 to 1 cm. or more with clear watery mucus and it is elongated, coiled, thin-walled, and fluctuating on palpation. Often a hard fibrous mass may be

palpated in the fimbrial area of the uterine tube. Hydrosalpinx may be observed in heifers; in these cases anomalies should be suspected. **Pyosalpinx** is less common than hydrosalpinx and usually occurs following severe uterine infections. Pyosalpinx is commonly associated with severe adhesions of the mesosalpinx and mesovarium. In pyosalpinx extensive perimetritis is not unusual. Pyosalpinx may follow the removal of a retained corpus luteum or the injection of large, slowly absorbed doses of estrogens for the treatment of pyometra. In rare instances the fimbrial end or pavilion of the uterine tube becomes attached around the edges and a large abscess or cyst may form between the bursa or pavilion and the ovary.

Mild cases of salpingitis have been described and found on histologic section but the oviduct is so small and the wall so thick that diagnosis of these minor cases of salpingitis cannot be made antemortem. Intramucosal cysts, cysts of the diverticula, (See Figure 133) have been observed in cows with a history of metritis and repeat breeding^{42,46} (See Figure 133). These may be seen grossly but cannot be palpated per rectum. These minute cysts result from a salpingitis where the epithelium of the free edges of the mucosal folds is denuded and these folds fuse. These cysts apparently do not prevent conception.

Diagnosis—The diagnosis of pathology of the uterine tube and ovarian bursa is difficult in most of the mild lesions. In severe, extensive lesions with marked adhesions involving the oviduct, ovary and adjacent structures the diagnosis is usually easily made. In the cow, cases of perimetritis and ovaritis, hydrosalpinx, pyosalpinx, and abscess or cyst in the ovarian bursa may be diagnosed by palpation per rectum. In hydrosalpinx the large, thin-walled, usually coiled and fluctuating uterine tube as well as the thickened area of adhesions causing the obstruction, can in most cases be felt by careful palpation (See Figures 131 and 132). In rare cases adhesions around the ovary may form as in pyosalpinx or a localized peritonitis, and the bursa or pavilion of the uterine tube may fill with clear mucus and resemble an abscess secondary to a suppurative pavilionitis with adhesions. When many severe adhesions are present it may be impossible to differentiate pyosalpinx or hydrosalpinx except on the basis of the history of the cow. In most cases adhesions resulting in hydrosalpinx are less pronounced than in pyosalpinx. Pyosalpinx is much less common than hydrosalpinx. In the milder cases of ovario-bursal adhesions 2 or 3 fingers may be inserted into the ovarian bursa and with the thumb placed on the outside of the bursa, the uterine tube and ovarian bursa can be palpated by rolling them between the fingers and thumb. Rectal palpation of the tube may also be per-

formed by carefully palpating the uterine horn to its apex and on to the oviduct to the ovarian bursa. Sometimes, working bimanually, the ovary is grasped with the vaginal hand the uterine tube and mesosalpinx are stretched caudally, making palpation easier. Palpation of the uterine tube per rectum requires experience and care. As noted from the references previously cited, only about 1/3 to 1/2 of the pathologic lesions of the oviduct and bursa are felt on palpation as compared to those observed on postmortem examination. The more frequent occurrence of pathology involving the right uterine tube and ovary is considered to be due to the fact that the right ovary is functionally more active. A greater number of slight adhesions from ovulations would be found between the bursa and ovary. Peritoneoscopy and visualization of the ovaries and uterine tube in the cow may be of diagnostic assistance in some cases.^{49,50}

The Rubin insufflation apparatus used widely in humans has been experimentally used in cows.^{56,92} After the cervix had been sealed, carbon dioxide was passed into the uterus under pressures of 60 to 100 mm. of Hg. If the uterine tubes were normal and open the pressure gradually fell to 40 to 60 mm. of Hg. This indicated that one or both uterine tubes were open. The escaping gas could usually be felt on rectal examination at the internal os of the oviduct or heard on auscultation as a gurgling or bubbling sound. The uterine tubes were distended up to 3 mm. in diameter and were firm. If the pressure failed to drop, this indicated that both tubes were obstructed. If it dropped rapidly this may signify that the air has penetrated the mucous membrane. Inserting a stethoscope into the rectum was recommended in order to hear the escape of the gas. Insufflation is not satisfactory at the time of estrum or immediately following estrum.⁵⁶ If this method is used during the diestrous stage of the cycle the danger of causing uterine infection must be considered. Presently there are no practical tests for obstructed uterine tubes in cows.

Prognosis. Generally this is considered guarded to poor in most severe cases of pathology of the uterine tube or bursa. Of 142 cases examined and diagnosed, 33 had bilateral lesions; of these, 30 were incurable and 3 eventually curable; of 109 which had unilateral lesions, 62 were curable, 36 eventually curable, and 11 probably curable.^{88b} In 84 cases with diffuse or extensive perimetritis, ovarian parametritis, caudal parametritis, hydrosalpinx, periophoritis, and closed bursae in which only 11 were bilateral, the conception rates were 13 to 40 percent.⁶⁷ In 349 cases in which 72 had bilateral involvement with mild lesions such as a narrow or shallow bursae, slight adhesions of the bursal borders, rough internal wall of the bursa, or thin threads of fibrous connective

tissue across the bursa, 63 to 79 percent of the cows conceived. In these cases about 75 to 80 percent were mild and the lesions noted had only moderate to slight adverse affects on the conception rate.⁶⁷ In 69 cases of cysts and nodules only 3 cases had complete obstruction of the tube.⁵⁶ Some quite strong adhesions were noted in pregnant cows. The prognosis in bilateral pyosalpinx and hydrosalpinx is hopeless. With conservative treatment and the passage of time, some acute conditions may markedly improve, with absorption of many adhesions, fibrin, and blood clots. Depending on the severity of the condition, the prognosis in chronic cases should be guarded to poor.

Treatment. The treatment of these conditions is in general not very satisfactory or specific. Some authors recommend the manual breaking-down of the chronic fine adhesions, while a few condemn this procedure as certain to produce greater adhesions. Treatment of pyometra or endometritis if present may prove helpful. Removal of a unilateral affected ovary and oviduct is of questionable value but it might improve the conception rate by having all subsequent ovulations be fertile ones.

Most authors do not approve of Rubin's insufflation method or similar methods for the treatment of cows because of the danger of rupturing the uterus and causing peritonitis especially if infection is present.

In general, conservative treatment such as mild, gentle massage of the uterus, possibly mild antibiotic douches or infusions of the uterus might be indicated together with a long period of sexual rest. In the mild salpingitis cases associated with an endometritis the former condition will usually correct itself spontaneously as the uterine endometrium returns to normal. Possibly systemic antibiotic treatment might be indicated in some cases.

The prevention of the pathology of the uterine tube, ovarian bursa, and ovary is more important than treatment. In treating retained placenta, metritis, or pyometra the use of large amounts of liquid, high pressures, and strong solutions should be avoided. Removal of the corpora lutea should be performed seldom, and only as a last resort. With the availability of the prostaglandins for luteolysis, manual removal of the corpus luteum should probably not be performed. Excessive, rough manipulation of the ovaries and oviducts should always be avoided, because once adhesions are produced they seldom disappear and may result in sterility and in the permanent loss of function of one or both ovaries. In areas where vigorous manipulation of the ovary and removal of cysts or corpora lutea are seldom performed and where conservative treatments of uterine infections is the practice, the incidence of diseases of the uterine tube have dropped markedly.

Uterus

Uterine pathology has been reported for many years as a cause of sterility and infertility.^{1,67,92} In recent years more work has been done and data are beginning to accumulate to indicate that the conclusions of these authors, largely based on clinical observations, were correct. These recent findings are substantiated by research into the bacterial causes of uterine infections and histologic sections of diseased uteri. This section of the chapter will consider uterine pathology including: endometritis, pyometra, mucometra, perimetritis, uterine abscess or abscess of the uterine wall, sclerotic metritis and uterine tumors. Previous sections of this text have covered acute or septic metritis, abortions, retained placenta, and postpartum metritis. A significant proportion of failures of conception have been ascribed to varying degrees of chronic metritis or endometritis. However it is important to note that the uterus and uterine tubes of the cow having estrous cycles have the ability to effectively eliminate specific or nonspecific infections within a varying period of time.

Endometritis due to uterine infection and secondary inflammation has been shown^{1,6,15,18a,b,c,27,30,31,34,37,41a,52,67,92} to be a common cause for infertility in cattle. Vibriosis provided the incentive and furthered this study (See Vibriosis and Trichomoniasis).

Etiology. All workers have shown that metritis and endometritis are likely to follow abnormal parturitions such as abortions, retained placenta, premature births, twin births, dystocia, septic metritis, postpartum metritis, pyometra and traumatic lesions or lacerations of the uterus, cervix, vagina or vulva. These factors are generally associated with a delayed involution of the uterus, chronic uterine discharge, slow recovery of the uterine endometrium, and delayed conception often associated with an increased number of services. In cows uterine infections and inflammations interfering with conception are likely to arise during even a normal calving period. As noted in Chapter VI and XI many bovine uteri become infected at the time of parturition and shortly thereafter. In the normal cow this infection is eliminated rapidly most commonly at the first or second estrus or ovulatory period.

Three reports have shown that, 90 to 100 percent of dairy cows have a uterine infection the first 10 to 15 days postpartum.^{27,30,31,93} This percentage declines to 30 percent by 30 to 40 days and to 10 to 20 percent by 60 days postpartum. These early uterine infections are usually a mixed culture of streptococci, staphylococci, *E. coli*, *Proteus*, *Pseudomonas*, *Corynebacterium pyogenes* mycoplasma, ureaplasma, *Hemophilus somnus*,^{41a} and others. Fertility was not affected by the mixed culture of

uterine flora or the endometritis present the first several weeks postpartum. However if *C. pyogenes* was present in the uterus after day 21 postpartum, especially if the infection persisted beyond day 50 with a delayed uterine involution, endometritis was severe and conception was usually delayed.³⁰ Transient infections of *C. pyogenes* during uterine involution did not affect fertility but transient *C. pyogenes* infections at a later period reduced fertility for one to three services whereas persistent *C. pyogenes* infections caused severe chronic endometritis or pyometra, and anestrus. Most cows that develop advanced endometritis and pyometra could be detected by rectal and more frequently vaginal examination before 42 days postpartum. Thus early and vigorous therapy to correct the endometritis could be instituted avoiding prolonged infections with severe endometrial lesions, pyometra and sterility.

Severe stretching or trauma to the vulva may occasionally cause "windsucking" or pneumovagina in cows. This is observed most often in older cows with a sunken anus and a nearly horizontal vulva (See Figure 135). The vulvar lips are often thin and atrophic. The vagina balloons, and air, feces, and urine (urovagina) may be drawn into the cranial portion of the vagina. In rare cases with chronic cervicitis or during estrum the uterus may become distended with air, causing a persistent endometritis as well as a cervicitis and vaginitis. The condition is similar to pneumovagina or urovagina in the mare and failure of conception, or "repeat breeding," is a frequent sequella.

Chronic uterine catarrh or endometritis may occur in cows and heifers following coitus. The importance and severity of trichomoniasis, vibriosis, mycoplasmosis ureaplasmosis and brucellosis have been discussed. The penetration of the uterine glands by *C. fetus* organisms has been well-described. For successful breeding results it is essential that these diseases be kept under control. The sheath of the bull usually contains many organisms of different types, and even though the introduction of antibiotics into the extended semen has proved helpful in controlling these organisms, it is of vital importance that the semen be collected in a clean manner, to prevent the possible introduction of many organisms into the cervix and uterus at the time of insemination. Insemination should be performed in a clean, sanitary manner and the semen deposited only in the cervix as infection may be introduced and established more readily by the intra-uterine deposition of semen. In ureaplasmosis and mycoplasmosis where ureaplasma and mycoplasma are often present in the caudal portions of the genital, some inseminators are using a sterile plastic tube introduced into the vagina and through which the AI pipette is passed to reduce the possibility of these organisms being intro-

duced into the uterus. Bulls with acute seminovesiculitis should not be used either naturally or artificially. In cattle the fairly tight, firm, mucus-filled cervix that assists in preventing infections from entering the uterus has great protective value. Besides the natural defenses against infection at the time of estrum in the cow, these factors help overcome the massive infection often introduced into the vulva and vagina at the time of natural service when little or no breeding hygiene is practiced. The more common streptococci, staphylococci, *C. pyogenes*, *Ps. aeruginosa*, *B. coli*, ureaplasma, mycoplasma and others may be secondary or accidental infections or contaminants. The severity of the endometritis is related to the type of organisms present. *C. pyogenes*, especially if it persists for long periods,^{27,30,85} causes severe endometritis as does *Br. abortus*.^{6,37} Whereas the other nonspecific organisms, or transient *C. pyogenes* infections cause no or only mild endometritis.^{27,30,85} Hemolytic types are generally more pathogenic than are nonhemolytic types. Since a variety of organisms may be introduced into the uterus or genital tract by various instruments or therapeutic practices, the inseminator and the veterinarian should use care, skill and cleanliness to prevent the possible introduction of infection whenever he inseminates, invades, examines, or treats the genital tract, especially the uterus. It is generally considered that unless much mucopurulent material is in the uterus probably fertilization would not be greatly affected but that normal development and attachment of the fertilized ovum in the uterus might be prevented, possibly temporarily by a variety of infectious organisms.

An extensive review of bacteriological studies of the normal nongravid and gravid bovine uteri over the past 60 years concluded that 20 to 40 percent of the non-gravid uteri contained bacteria, largely micrococci, streptococci, and occasionally *E. coli* and others.³⁴ The studies on the normal gravid uteri were less conclusive as positive bacterial cultures, with organisms similar to those found in the nongravid uteri varied from 2.5 to 88.7 percent. The uterine microflora of subfertile or sterile cattle was also reviewed and investigated. Although this review indicated that nonspecific infections of micrococci, streptococci, *C. pyogenes*, *Pseudomonas aeruginosa* and others may be responsible for bovine reproductive failures by causing metritis or endometritis in from 5 to 55 percent of cows, they played only a minor role in reproductive failures in "symptomless repeat breeders." This was indirectly confirmed by field trials with a wide variety of antibiotic and antiseptic preparations infused into the uteri of repeat breeders without a significant improvement in conception rates from control cattle. **Endometritis was shown not to be a major cause of reproductive failure in symptomless subfer-**

tile cows.³⁴ Thus one can conclude that if an endometritis is present due to a variety of possible organisms including viruses that infertility will occur in direct relationship to the severity of the endometrial lesions and the pathogenicity of the organism. If an endometritis is not present, a few nonspecific contaminating organisms present in the uterus, or introduced into the uterus by their presence in semen or on the intrauterine pipette will not have an adverse effect on fertility.

Biopsy of the uterine endometrium and submucosa found 70 percent of 110 sterile cows showing some degree of endometritis. Of these 110 cows 45, or 41 percent, had lesions sufficiently severe to probably prevent conception at the time the biopsies were taken.⁶ Of 82 sterile cows whose uteri were biopsied and cultured, 38, or 46 percent, had both infectious organisms and an endometritis present.³⁷ Most of the earlier clinical workers reported a higher incidence of infection because cultures were from the cervix or external portions of the cervix. Newer instruments and techniques have enabled workers to obtain samples from the uterus relatively free of cervical contamination.^{23,67} As a result these authors have reported a lower incidence of true uterine infections. Mixed cultures from the vagina or external portion of the cervix are common but pure cultures are frequently obtained in uterine cultures.³⁷

Signs. The clinical symptoms of an endometritis often cannot be demonstrated by rectal or vaginal examination. In the more severe cases there may be a mucopurulent discharge from the uterus in the vagina. Vaginal examination is important for the detection of a uterine exudate indicative of endometritis.^{51,85,87} At the time of estrum flakes of pus in the estrual mucus indicate a possible endometritis. The source of these flakes may be difficult to delineate clinically inasmuch as they may come from the vagina, cervix or uterus. The mucus of estrum may be cloudy or milky instead of clear or translucent and contain many leucocytes when endometritis is present.^{51,71} Bovine cervical mucus in proestrus may normally be slightly cloudy. In many cases a mild to definite cervicitis may be present with an endometritis or be secondary to it due to contamination from the uterus. In some cases douching of the uterus may wash out flakes of mucopurulent material and then the diagnosis is more certain. Massaging the uterus during estrus often will expel mucus into the vagina so it may be examined.⁸⁵ The seriousness of endometritis cannot be diagnosed from clinical manifestations except in cases in which purulent material is present or discharged. On rectal examination the uterus may occasionally feel slightly large, heavy, and thick-walled. These changes may be limited to one horn, possibly the gravid horn of the prior pregnancy. This evidence of failure of normal, prompt involution of

the uterus may accompany chronic endometritis and uterine infection. However diagnosis on the basis of a rectal examination is not reliable. The estrous cycle and periods are usually normal in length. In occasional cases the cycle may be shortened to 8 to 12 days due to acute endometrial inflammation preventing the development of a normal corpus luteum probably by the secretion of prostaglandin. Because of the abnormal endometrium and infection in the uterus the early embryo may die and the cow again come into estrus. The usually prolonged estrous cycle may vary in length due to early death and maceration of the embryo as in trichomoniasis, vibriosis, and possibly other infections. Repeated services and failure of conception may be common symptoms of endometritis. Because many or all of the above clinical symptoms are at times variable and frequently absent, with the exception of failure of conception following repeated services to a fertile bull or with fertile semen, accurate diagnosis in the field at present is often impossible. A careful examination and biopsy may eliminate other possible causes of infertility and the diagnosis of possible endometritis may be arrived at by a process of elimination or laboratory diagnosis by culture and histopathologic examination of carefully obtained and processed biopsy material. The most common lesions found in endometritis in cattle, were exudation, a periglandular fibrosis with leukocytic cellular infiltration and subsequent glandular degeneration and dilation.⁵²

The use of special equipment for culturing and taking a biopsy of the uterus in the clinical patient have been developed for cows,^{6,23,38,53,55,67,82} plus certain instruments used in treating humans, have made possible the further study of endometritis. For practical reasons this equipment together with some special equipment used for diagnosing vibriosis and trichomoniasis probably can only be used to a limited extent in the field, but it can be used for special diagnostic and research work on this important phase of sterility or infertility. In a study on 110 sterile cows, 27, or 87 percent, of 31 cows that showed some clinically diagnosable abnormalities had an endometritis.⁶² In 79 sterile cows without clinically detectable abnormalities 50, or 63 percent, had endometritis. The endometritis was generally more severe in the first group. It was found that slight cases of endometritis diagnosed by biopsy did not interfere with conception; therefore if these cows were eliminated from the above groups the percentage in each group having endometritis severe enough to cause sterility or infertility would be 57 and 37 percent, respectively. A group of 54 cows that had not been inseminated or served since their last calving were examined. Only 11 had been in estrus; 42 showed clinical abnormalities, mainly poor involution of the uterus; and on biopsy 50 of the 54 had evidence of

endometritis. The lesions were more severe the nearer the biopsy was taken to the time of calving. In general, lesions were more severe in cows that had not been in estrus. Inflammatory lesions were more likely to be found in the larger horn of the uterus if the horns were unequal in size.⁶ On the basis of biopsy examinations predictions could be made on the approximate time necessary before the inflammatory reaction would subside sufficiently so that conception could be expected.⁶ An excellent study reported that most abnormalities of the uterus including infection and endometritis recover spontaneously during involution of the uterus, and latent endometritis is not often responsible for reproductive failures in clinically normal cows.¹⁷ Because of the usual prompt natural recovery of endometritis in the involuting uterus, intrauterine infusions of antibiotics were of limited value. Of 99 cows examined at 10 days and 20 days postpartum and at the time of the first insemination, intrauterine infection was present in 49, 25, and 3 percent, respectively.¹⁷ Endometrial biopsy studies at various stages of the estrous cycle in normal cattle showed that such a procedure was safe and had no effect on fertility. Biopsies of the endometrium should be taken from the medial wall of the uterine horn by a suitable biopsy forcep.^{71,82}

Prognosis. The prognosis in most cases of endometritis is fair to good. With each repeated estrous cycle the natural body-defenses and the changes produced within the uterus and the genital tract by the estrogens tend to aid recovery. Thus endometritis is seldom static; nearly all cases recover spontaneously with the passage of a variable period of time and sequential estrous periods. Endometritis due to persistent infections of *C. pyogenes* or brucella have a more guarded prognosis. This effect of the estrous period in assisting in the elimination of infection has been described.^{3,32,37,78} This work showed that infection introduced into the normal uterus at the time of estrus was rapidly overcome and did not establish itself. When infection was introduced during the progestational phases of the cycle it more easily became established and pyometra might result. Of 463 cases of cows suffering from a purulent postpartum discharge without pyometra, 87 percent conceived after treatment.⁶⁷ In 111 infertile cows bred 2 or more times before taking a biopsy of the endometrium, the following results were reported;⁶ (see table, next column).

Endometritis, as other inflammatory processes in the body, tends to recover spontaneously. The more severe the endometritis the longer the time required for recovery. Slight endometritis may not prevent conception and from a biopsy the approximate length of time for recovery could be estimated.^{6,85}

Treatment—There are many therapeutic agents and procedures, used and advocated for the treatment of en-

Degree of Endometritis	Number of Cows	Percent- age Con- ceiving First Service After Biopsy	Percent- age of Total Con- ceptions	Services per Con- ception
None	27	74	85	1.57
Slight	31	74	90	1.36
Moderate	25	48	80	1.70
Severe	28	11	60	3.77

dometritis. If rectal and vaginal examinations and a clear vaginal mucus indicate a normal involuted uterus, there probably is not sufficient endometritis to cause repeat breeding or failure of conception due to an endometritis. However, until controlled experiments are performed using biopsy and cultural methods on large numbers of infertile or "repeat breeding" cows to define the severity of the endometritis (if this is the cause for the sign of failure of conception) and compare the various treatments, it cannot be stated with authority which treatment is superior, or whether the complete omission of treatment may not be best.⁸⁵ Routine biopsies and cultures of the bovine uterus, are not practical but are indicated in specific herd or individual cow problems. In vibriosis and trichomoniasis the development of a local immunity will in a few months overcome the intrauterine infection and produce recovery so conception can occur. When ureaplasma or T strain mycoplasma were introduced into the uterus, an endometritis and salpingitis developed but the uterus rapidly eliminated the infection within 10 days.¹⁸ It is likely that other accidentally introduced pathogens would share a similar fate. Most treatments are based on either promoting estrous cycling and/or overcoming the suspected or known intrauterine infection.

The treatments used to stimulate the muscle tone, blood supply, and flow of mucus of the uterus are varied. Regular warm-to-hot, mild antiseptic solutions such as the aromatic soap solutions, mild quaternary ammonium, neutral iodophor, or chlorine solutions, physiological saline, dilute potassium permanganate solutions, sodium bicarbonate solutions, weak "Lysol" solutions, and dilute iodine or **Betadine** solutions may be used in 500 to 4000 ml amounts as vaginal douches. Mild, gentle uterine massage per rectum 2 to 3 times a week may possibly be of value in producing similar effects. Applying 1 percent acriflavine ointment on the external os of the cervix and cranial portion of the vagina by massage, swabbing the cervix with Lugol's solution or other irritating iodine-base cervicitis mixture may also stimulate circula-

tion, uterine tone, peristalsis, and the secretion of mucus by the endometrium.

Either intramuscular injections or intrauterine infusions of estrogens alone or combined with antibiotics are presently seldom used because both are not recommended for use in lactating dairy cows because they are eliminated in the milk. Possibly repeated treatments with prostaglandins at 10 to 12 day intervals might hasten recovery of an endometritis by causing frequent recurring estrous periods.⁷⁰

Intrauterine infusions or douching of the uterus with

an irritant antiseptic such as dilute iodine solution, 2 ml. of Lugol's solution in 100 ml of water, will strongly stimulate uterine muscle contraction and tone and greatly increase mucous secretions. In fact, douching the uterus with any fluid including saline, acriflavine solutions, 1:500 to 1:3000 concentrations, chlorine, 200 ppm, chlorhexidine, or 200 ppm **Betadine** solutions or other antiseptics probably has a mild irritating action on the endometrium, results in the mobilization of leucocytes, stimulates uterine motility, and has an antiseptic and flushing action on any mucopurulent material. It is desirable to

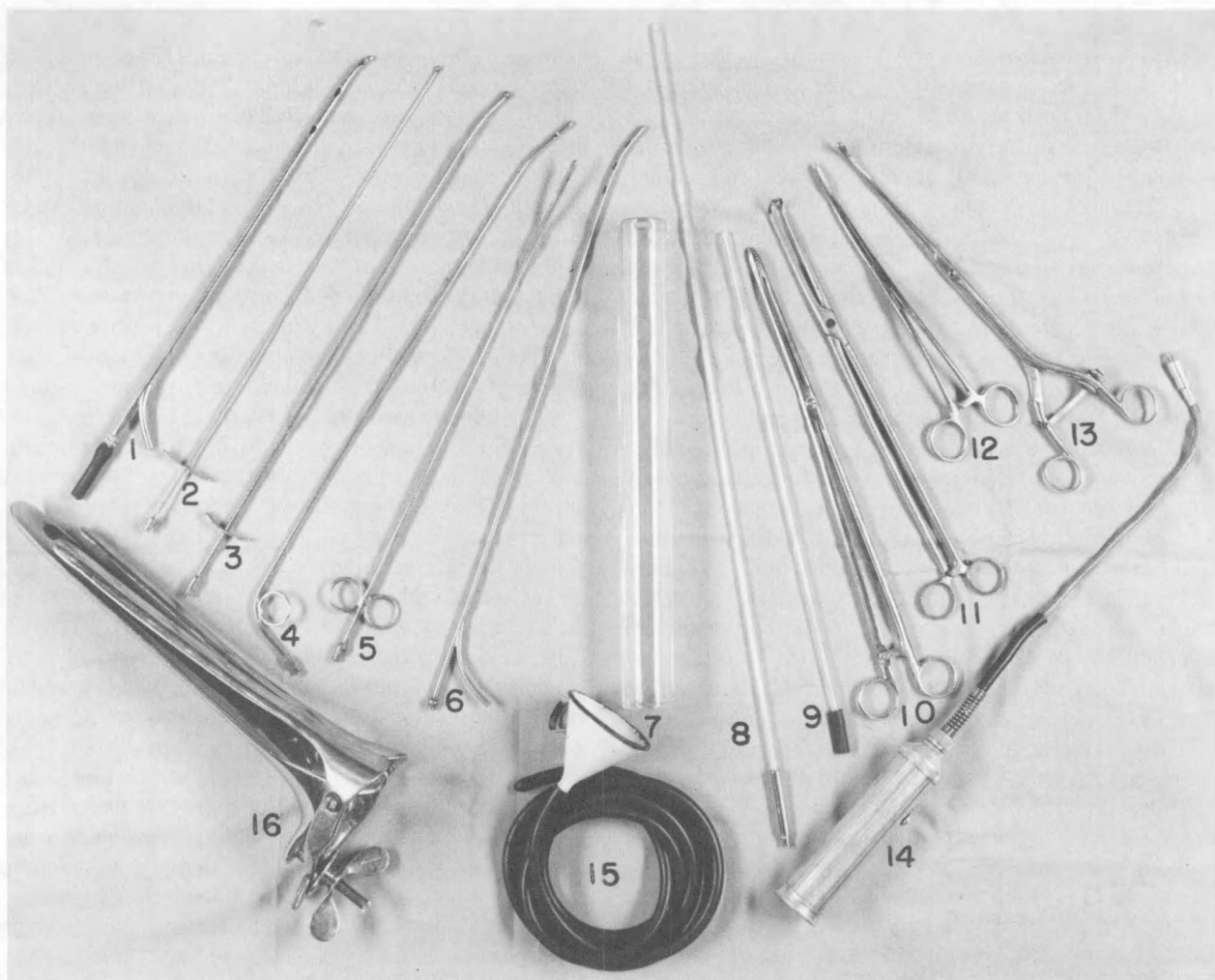


Figure 134. Some Common Instruments Used in the Treatment of Infertility in the Cow and Mare.

1. Smith Uterine Catheter with Rubber Adapter. 2. Luken's Intrauterine Infusion Catheter. 3. Chambers' Intrauterine Infusion Catheter. 4. Woelffer's Intrauterine Infusion Catheter. 5. Nielsen's Intrauterine Infusion Catheter. 6. Small Uterine Catheter for Douching. 7. Glass or Plastic Vaginal Speculum. 8. Long Plastic Insemination Pipette with metal adapter for the mare. 9. Insemination pipette with rubber adapter. 10. Knowles' Cervical Forceps. 11. Hopper's Cervical Forceps. 12. Long Dressing Forceps. 13. Palmer's Cervical Dilators. 14. Flexible Extension Flashlight. 15. Rubber Horse Catheter and Funnel. 16. Caslick's Vaginal Speculum for the Mare.

infuse a mildly irritating chemical such as an iodine solution or certain antiseptics during the follicular or estrous phase of the estrous cycle to avoid a prolonged estrous cycle, 24 days, as may occur if the infusion is administered during late diestrus, about day 15, or a shortened estrous cycle of 8 to 10 days if the solution is administered about day 4 of the diestrus or luteal phase of the cycle.^{65,71,80}

By a combination of rectal manipulation of the cervix and the vaginal introduction of a 2-way-flow catheter of small diameter, the catheter or AI pipette can be passed into the uterus. By means of a funnel and tube, an intravenous outfit, a large syringe or a pressure bulb outfit attached to the end of the catheter, the douche or infusion solution is run into the uterus. This is most easily accomplished in heifers and cows at the time of estrum. If a cervicitis is present or an enlarged uterus has dropped down into the abdominal cavity, Knowles's or Hopper's cervical forceps may be applied to the cervix to pull it back toward the vulva. With the uterus and cervix pulled back by the forceps, one hand can grasp the cervix in the vagina and with the aid of a uterine catheter, or an AI plastic pipette in a rubber horse catheter to provide stiffness, the latter may be inserted into the uterus. After douching or infusing the uterus the cervix may be swabbed with gauze soaked in a strong antiseptic and fastened securely on a pair of narrow dressing forceps. Care should be used in passing the catheter through the transverse folds of the cervix and into the uterus so that neither of these organs is injured or ruptured. As an aid to passing the catheter or pipette, the rectal hand should grasp the cervix and push it forward to obliterate the folds in the vaginal wall. As the catheter is being gently passed through the cervix, the cervix should be manipulated in various directions to help "thread" it over the pipette. During the operation the cow should be well-restrained. Although douching the uterus with a metal catheter or infusing antibiotics or antiseptics into the uterus with a catheter or pipette usually causes no harm, great care should be exercised so that the uterus is not injured or perforated by the catheter and thereby producing more damage than any possible good that could be derived from the infusion. Infusing fluid in excess of 100 ml into the nonpregnant uterus of a heifer or more than 150 ml into a cow's uterus may rupture the uterus or force the fluid into the tissues of the uterus.⁸³ It was impossible to force fluid through the uterine tubes as rupture of the uterine endometrium occurred and the fluid passed between the peritoneal coverings of the uterus. If more than this amount of fluid is infused some of it should be allowed to flow out through the cervix. A spiralled indwelling plastic uterine infusing instrument was de-

scribed³⁸ that could be passed through the cervix into the uterus and it would remain in place so that repeated twice daily or daily infusions could be given without reinserting a pipette. This instrument if left in place for a period of time acts like an I.U.D. resulting in shortened cycles. Further study is necessary to ascertain its value and whether or not endometrial damage may result from prolonged retention in the uterus. Presently their use has not become generally accepted.

Other treatments have been used for endometritis with the idea that if the infection is overcome the endometritis will heal more promptly and the infertility will be overcome more rapidly. These treatments include the intra-uterine infusion of antibiotics such as: penicillin, streptomycin, **Aureomycin**, **Terramycin**, tetracycline, tyrothricin, neomycin, **Chloromycetin**, tylosin, furacin preparations, polymyxin, and others, alone or in combination, incorporated in saline solution, distilled water, oil, sodium sulfonamide solutions, or oil-in-water emulsions. The tetracycline preparations have been recommended for the treatment of mycoplasmosis or ureaplasmosis.¹⁸ Many veterinarians will infuse intramammary products with a broad-range of antibiotic activity into the uterus by means of a uterine pipette. Usually 500,000 to 1 million units of penicillin and 0.5 to 1 gm of streptomycin or 0.5 to 1 gm of the broad range antibiotics are infused in 10 to 50 ml of vehicle. Large doses of antibiotics infused into the uterus will result in their elimination in the milk. So milk should be withheld from the market for the proper period of time, approximately 24 to 48 hours.⁸⁰ The treatments using penicillin and streptomycin in saline or distilled water may be given within 3 to 6 hours before service. The other antibiotics or vehicles are usually given within 24 to 36 hours after insemination or breeding as they have a harmful effect on spermatozoa if administered shortly before service. By infusing the uterus at this time if bacterial infections are present they will be eliminated or reduced so the uterine environment for the fertilized ovum when it arrives several days later will be conducive in for its survival and growth. Infusing the uterus during estrum may result in some of the infusion escaping through the dilated cervix. For this reason infusing aqueous easily absorbed solutions during the luteal phase of the cycle has been recommended.⁷ Although more endometrial reaction to infusions occurs during the luteal phase of the cycle,⁸⁹ the author and others have observed no definite harmful effects from such a practice unless irritating solutions are given from 2 to 6 days or 12 to 17 days of diestrus and result in a shortening or lengthening of the cycle.

Weak Lugols' solution is quite irritating to the endo-

metrium. The author has used a weak Lugols' solution, 2 ml/100 ml of saline, at doses of 20 to 50 ml infused into the uterus from 12 to 36 hours post service for many years without reducing conception rates on the preceding or subsequent service, or causing luteolysis with a short 8 to 10 day cycle. The results of using this weak iodine solution have equalled or exceeded the results with other antibiotic or antiseptic products or mixtures. The effectiveness of antibiotic preparations is not known. In vibriosis a few limited experiments have been conducted on the effects of antibiotics, especially dihydrostreptomycin, on campylobacter organisms *in vivo* but the results, although not discouraging, leave much to be desired. More work on the value of these preparations will have to be done under controlled conditions to arrive at a true evaluation of the benefits derived.

Iodine is rapidly absorbed from the uterus. Its beneficial action may be due to its microbiocidal activity, the local irritation, leucocytosis, and hyperemia it produces; and it may correct an iodine deficiency.²⁰ Empirically providing iodine improved fertility.^{56b} The use of mixed bacterins, the oral feeding of sulfonamides, or iodide preparations are of questionable or no value.

If a **chronic pneumovagina or "windsucking" condition** is present due to a tipped or nearly horizontal flaccid vulva, and a vaginitis and probable metritis with repeated services occurs, it is necessary to scarify and suture the vulva in a manner similar to that described for Caslick's operation in the mare. (See Figures 142 and 85.) Interrupted vertical mattress sutures should be used, since skin clips are usually rubbed out by the cow's tail. Antibiotics applied locally to the uterus and vagina, and sexual rest may be indicated in these cases. After one to 4 normal estrous cycles, artificial insemination is performed. The author has had a high degree of success with this therapy when it was indicated. Urovagina (urine pooling) is rarely observed in cows. The condition requires surgical correction to restore fertility.

In the past many reports on the value of certain infusion products or treatments for failure of conception due presumably to endometritis or uterine infections have appeared in the literature.^{74a} Most of these reports proved nothing more than the fact that most cows respond to whatever treatment was used. Very few of the experiments included control animals and when they did the numbers were not sufficiently large. This is to be expected when work of this type must be done in a field practice where controlled conditions usually are difficult to establish. Whenever such a wide variety of treatments is reported as being successful, it indicates that no treatment would probably show similar results. From the figures the author cited in 1956 it was evident that any ef-

fective treatment of "repeat breeders" due to a possible endometritis must raise conception rates on the next service to well over 50 percent. No such treatment has been reported. Most cases of uterine infection and endometritis recover spontaneously.^{6,17} Sexual rest is indicated for cows with obvious and severe endometritis. In the suspected case of endometritis in the "repeat breeding" cow without any obvious symptoms, conceptions would probably occur sooner if breeding was continued rather than suspended. If the bull is to be conserved, then sexual rest for a month or so in these "repeat breeding" cows may be indicated. There is no evidence that repeated natural service or insemination into the cervix causes any delay in recovery from possible endometritis.

The Prevention of Endometritis or reducing the problem to a minimum requires proper care, sanitation, management, and handling of cows at the time of parturition and the early postpartum period to prevent infections of the uterus (See Chapter VI and XI). If infections occur, prompt and—if necessary—repeated treatments at 1- to 2-week intervals are indicated. Conservative treatment of retained placenta and postpartum uterine infections is usually desirable. If pneumovagina is present prompt closure of the vulva is indicated. Brucellosis, vibriosis, and trichomoniasis should be controlled. If artificial insemination is employed the semen should be free of possible infectious agents and be deposited in clean manner in the cranial portion of the cervix and not into the uterine horn. Vaginal examinations and uterine and vaginal treatments should be conducted in a clean, hygienic manner to prevent the introduction of infection.

Delayed postpartum involution of the uterus is seen most often in older pluriparous cows during the Fall and Winter months and especially in cows with abnormal parturitions including: dystocia, retained placenta, acute metritis, prolapse of the uterus, and cesarean section. Delayed involution was most noticeable the first 30 days postpartum⁶⁰⁻⁶² (See Chapters VI and XI). In general cows with abnormal parturitions required about 5 days longer for their uteri to involute than did cows calving normally. Severe uterine infections definitely retarded the rate of involution. An enlarged uterus 30 to 60 days postpartum is often diagnosed clinically by many veterinarians as having chronic endometritis. The disease condition(s) occurring at parturition and the length of the postpartum interval prior to breeding were of greater importance in determining the conception rate on first service than was the involutionary state of the uterus based on a rectal examination after 30 days postpartum in cows with a grossly normal uterus. This examination was conducted on 1634 cows at 30 to 50 days postpartum.⁸⁷ The

presence of a mucopurulent exudate in the vagina was considered diagnostic for the presence of an endometritis. Infertility was independent of uterine size, and delayed involution in the absence of disease was unimportant. The presence of endometritis had only a slight influence on uterine size and could not be diagnosed by rectal palpation alone. The average calving interval was 10 days longer, 394 days, for cows with endometritis than it was for the normal cows and conception rate on first service was 12 percent lower. Preventive therapy for postpartum endometritis of 2 gm oxytetracycline or neomycin placed into the uterus immediately after the placenta was dropped was of no value and even delayed conception and reduced fertility in 2 groups of 75 cows each compared to 79 controls.^{35a} Conception rate after first service, after 3 services and the number of breedings per conception were 49, 40 and 60 percent, 73.3, 72.9 and 85.3 percent and 2.24, 2.56 and 1.67 respectively. A recent controlled study with neomycin boluses came to the same conclusion.²⁴ Infusing cows' uteri 20 to 40 days after calving with 100 mg of oxytetracycline as an aid in controlling endometritis did not improve fertility.²⁵ Uterine infusions of antibiotics in the postpartum period were not advantageous.¹⁷ Conversely cows with clinically evident endometritis by the presence of a cloudy mucus had much lower conception rates than normal cows, 7 to 11 percent, vs 55 to 75 percent, respectively.⁷¹ When a large number of cows were infused with an antibiotic mixture of penicillin, chloromycetin and sulfonamide 24 hours after first service, the conception rate was 53.3 percent compared to 23.2 percent for untreated controls.⁷¹

In an extensive field trial of 3582 cows in 9 herds in California⁵¹ in which the cows were examined between 21 and 35 days postpartum and placed in 3 groups, normal, moderate endometritis and severe endometritis based on clinical examination by palpation of the uterus per rectum and for the presence of a uterine or vaginal exudate by a vaginal examination. The cows in the former group were not treated and the cows in the latter group were treated with several intrauterine infusions of antibiotics. The middle group with moderate evidence of endometritis alternate cows were infused with antibiotics into the uterus or not treated and kept as controls.⁵¹ There was no difference in the subsequent fertility between the normal or moderate endometritis groups. In the latter the results were similar for controls and treated cows. The group with severe endometritis had a significantly lower conception rate and a higher number of days open. A total of 216 cows in the moderate endometritis group were selected for bacteriologic and pathologic examination; 32.4 percent were positive on culture and 26 per-

cent had an endometritis with an inflammation of the endometrium. Thirty eight or 54 percent of the cultures were positive for *C. pyogenes* with nearly a 100 percent correlation between the culture of *C. pyogenes* and the presence of an endometritis. There were only 2.7 percent of cases where endometritis was present with no bacterial isolation. Cows in which other organisms such as streptococci, staphylococci and *E. coli* were cultured only had a 30 to 50 percent incidence of endometrial lesions. In this study the vaginal examination for the presence of a uterine exudate was more accurate in the diagnosis of endometritis than the rectal examination.⁵¹ The efficacy of the antibiotic therapy used was unable to be evaluated in this study.

If delayed involution is obviously accompanied by a chronic metritis or endometritis as noted by a mucopurulent discharge from the uterus or the presence of a variable amount of exudate in the uterus at 20 to 40 days postpartum, treatment as outlined in postpartum metritis or pyometra is indicated. The interval between calving and breeding should be extended in affected, diseased cows.

The author has observed that pluriparous cows with a long mesometrium and a deep abdominal cavity permitting the uterus and cervix to be located some distance below the pelvic floor tend to have a larger, heavier, thicker uterus and cervix and be less fertile than cows whose uterus and cervix is located higher in the abdominal cavity on a level, with the pelvic floor. Uterine lochia or infectious material drains out earlier and more completely and possibly the circulation to the uterus is improved resulting in less edema or passive congestion in the latter cows. The author has even considered the possibility of attempting to fasten the cervix in the pelvic cavity in some severely affected cows.

Endometritis whether due to a venereal disease, vibriosis, trichomoniasis, and brucellosis, or due to a transient uterine infection with a variety of organisms including streptococci, staphylococci, coliform organisms, mycoplasma, *Hemophilus somnus*, ureaplasma or even *C. pyogenes* following parturition, service, either AI or natural, or accidental invasion from the caudal genital tract secondary to a vaginitis or cervicitis does result in infertility, failure of conception and a prolonged postpartum interval to conception. Thus regular postpartum rectal and vaginal examinations should be practiced starting at 15 days postpartum, but especially at 30 to 40 days, to detect persistent or chronic uterine infections resulting in delayed uterine involution and infertility. Prompt, early and monitored treatments should be undertaken to correct the pathological condition as rapidly as possible. Venereal diseases should be prevented or

controlled. If repeated services at regular or irregular intervals occur, careful examinations, possibly supplemented by biopsy or culture procedures should be undertaken as well as a careful review of management, heat detection, and insemination or breeding practices. From the theoretical view the author agrees with his potential critics that treatment of the normal cycling or repeat breeding cows is probably unnecessary and possibly contraindicated.^{12,85} However the practical on-the-farm situation invariably calls for some type of therapy based on a clinical examination of the cow which is not always definitive. Therefore treatment is often administered or advised based on the veterinarians best judgment and perception of the problem. The treatment recommended or utilized however should not be detrimental to the cow, her chances for conceiving promptly, and the cost-benefit ratio should favor the owner.

Pyometra in cattle is characterized by the accumulation of pus or mucopurulent matter in the uterus, and by a retained corpus luteum with failure of estrum due to suppression of the endometrial luteolytic factor or prostaglandin secondary to the severe endometritis. Some authors consider any accumulation of pus or mucopurulent exudate in the uterus even though the animal has estrous cycles as pyometra. This author adheres to the former definition and terms the latter a metritis or endometritis. Uterine distention does not cause anestrus.²⁹ The retained corpus luteum is not the corpus luteum of pregnancy in postpartum pyometra but is the corpus luteum following the first to third ovulation that persists due to the uterine infection associated with endometrial pathology. Pyometra usually occurs following an abnormal parturition, a uterine infection, and a tardy involution of the uterus in such conditions as abortion, premature birth, twin birth, dystocia, retained placenta, septic metritis, or postpartum metritis (See Figure 135). True pyometra seldom recovers spontaneously. Some veterinarians speak of pyometra as the chronic mucopurulent discharge seen for 2 to 3 weeks following calving due to a postpartum metritis. In a narrow sense this may be correct since there is pus in the uterus, but most of these cases come into estrum, cycle regularly, and the pus is expelled within 30 to 60 days after parturition. True pyometra exists for 60 to 90 or more days after parturition with a failure of estrum. It may occasionally follow service and when it does it is usually associated with the early death and maceration of the embryo and its membranes. In these cases trichomoniasis should always be suspected and the pus examined for trichomonads. Other infections due to a variety of organisms, most frequently *C. pyogenes*, may also cause death of the embryo and pyometra, or be a secondary invader. Occa-

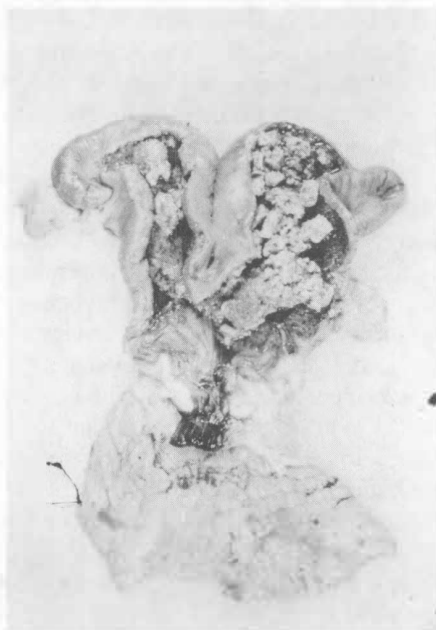


Figure 135. Chronic Postpartum Metritis and Pyometra due to In-spissated Necrotic Cotyledons and Caruncles.

sionally pyometra may be produced by the insertion of an inseminating pipette into the uterus of a pregnant cow that may have shown symptoms of estrum. Infection introduced in the semen or by the operation causes the death of the embryo, its maceration, and pyometra. This condition occurs more commonly when the semen contains no antibiotics. In rare instances pyometra may develop secondary to mucometra in a heifer with an imperforate hymen that has been bred by a bull or artificially and infection is introduced into the genital tract distended with the mucus or it may develop secondary to mucometra caused by chronic cystic ovaries.

Symptoms—Pyometra is characterized by the failure of estrum, a persistence of the corpus luteum, and the retention of pus or mucopurulent material in the uterus. The amount of this pus may vary from 2 or 3 ounces to 2 to 4 gallons. In most cases of postpartum pyometra the cervix is relaxed so that some of the pus escapes and is observed occasionally when the cow lies down, urinates, or defecates. On examination 3 to 4 ounces of pus are frequently found in the cranial portion of the vagina. The pus is usually thick mucoid and creamy, and yellow, white, or greenish-gray in color. In 67 cases of pyometra recorded by the author in an area where trichomoniasis was not seen, a mucopurulent discharge was observed by the owner in 57, or 86.6 percent, of the cases on various occasions before the condition was diagnosed and

treated. On rectal examination the uterine wall is usually thickened, flaccid, and atonic. The pus that distends the uterus may simulate pregnancy but the consistency of the pus is heavy and not watery like normal placental fluids. Pinching of the uterine wall does not reveal the slipping of the fetal membranes as in pregnancy. The fetal cotyledons, and enlarged whirling uterine artery of a normal pregnancy are not palpable in pyometra. The bovine animal rarely shows any signs of systemic illness even when gallons of pus may be in the uterus. If on the first examination, the diagnosis of pyometra cannot definitely be made, reexamination in 20 to 30 days will reveal a failure of normal developmental changes characteristic of pregnancy. Passing a metal catheter through the cervix will remove some pus, or an injection of 25 to 40 mg. prostaglandin F_{2a} or 500 ug cloprostenol will probably cause the evacuation or release of the pus from the uterus. A white-blood-cell count is of no value in diagnosing pyometra in the cow.

Prognosis—The earlier a case of pyometra is diagnosed and treated, the greater the possibility of its successful correction or cure. In long-standing cases the endometrium is destroyed, the uterine wall undergoes fibrotic changes, and in some cases complete recovery and conception cannot occur. In the cases that have existed for only 60 to 120 days, recovery and conception are more likely than in cases present for 120 days or longer. The type of organism and its effect on the endometrium and uterus play an important role. *C. pyogenes* is commonly found in severe or incurable cases. Recovery in cases with over 2 gallons of pus in the uterus seldom occurs because of the degenerative changes in the uterine wall, producing a marked lack of tone. Recovery of cases of pyometra associated with severe perimetritis is hopeless. In a series of 35 cases of pyometra 51.4 percent of the cases conceived.⁶⁷ The author in a series of 67 cases recorded a conception rate of 46.3 percent.⁷⁵

Treatment—The treatment consists of producing an involution of the retained corpus luteum so that the estrous cycle is reestablished, the cervix will dilate, the uterus will contract and the pus will be evacuated. The induction of estrus may be brought about by the injection of 20 to 40 mg of prostaglandin F_{2a} (**Lutalyse**) or 500 ug cloprostenol (**Estrumate**) intramuscularly. Douching the uterus with a horse catheter, draining the pus from the uterus, injecting antibiotics, and massaging may in rare cases produce recovery but the other procedures are much more effective in establishing a prompt return to the regular estrous cycle necessary for recovery. Excessive massage of the uterus should be avoided, as perimetritis and adhesions may occur.

In the past, manual removal of the corpus luteum was

practiced. Since these corpora lutea associated with a pyometra were retained or persistent they were difficult to enucleate and hemorrhage and/or extensive adhesions frequently resulted. Estrogens such as estradiol and stilbestrol were formerly used to involute the corpus luteum. Large and often repeated doses of estradiol, 8 to 10 mg., or stilbestrol, 80 to 100 mg, were necessary. Occasionally cystic ovaries or severe ovaritis and adhesions of the fimbria resulted. Oxytocin alone or combined with the estrogens or prostaglandins has not proven to be of value.⁷⁵ If the first dose of prostaglandin does not completely involute the C.L. and evacuation of the uterus is not complete, the treatment should be repeated in 10 to 12 days. In a total of 42 cows with pyometra treated with a luteolytic dose of either PGF_{2a} (**Lutalyse**) or cloprostenol (**Estrumate**) 90 to 100 percent of the cows showed estrus by the third day and discharged copious amounts of pus from 3 to 5 days after the injection.^{28,70,91} At 12 to 14 days later the uterus was completely evacuated in nearly all the cows. About 65 percent of the cows conceived after 2 or more (2.2 average) inseminations. In a large recent study^{21a} of pyometra or pyometritis in postpartum dairy cows 72 of 79 cows (95%) and 57 of 73 cows (78%) evacuated the purulent exudate from their uteri after one or two treatments 7 to 10 days apart of 500 ug cloprostenol and 7 to 12 mg estradiol cypionate, respectively. Treatment to breeding and treatment to conception intervals were similar for both treatments. Recurrence of pyometra developed in 9 and 5 percent of treated cows; follicular cysts developed in 16 and 7 percent and perimetritis and adhesions developed in 2 and 5 percent, respectively. Treatment with nitrofurazone was of no value in preventing relapses or improving conception rates.^{21a}

After treatment and expulsion of the pus from the uterus and the establishment of normal estrous cycles the cows should not be rebred for several normal estrous periods. Before breeding is permitted the uterus should return to its normal size and consistency and no metritis or cervicitis should be present. The use of antibiotic infusions or other therapy as described under endometritis may be of some value in hastening recovery.

It is rather obvious that pyometra can produce severe damage to the endometrium that either prevents conception even though the pus is evacuated, or delays conception so that the owner sells the cow as unprofitable. To prevent pyometra, cows having a postpartum mucopurulent discharge should be treated promptly to hasten involution of the uterus.⁵⁹ Insemination into the pregnant uterus and breeding to trichomonad-infected bulls should be avoided.

Perimetritis and Parametritis are observed occa-

sionally in the cow and are characterized by varying amounts of adhesions between the uterus and broad ligaments and the other pelvic and abdominal organs. (See Figure 136.) Endometritis and metritis are inflammations of the endometrium and the entire thickness of the uterus. Perimetritis and parametritis involve inflammation of the serosa and uterine ligaments, respectively. Adhesions associated with or secondary to inflammation are usually secondary to one of the following: a severe septic metritis; douching and perforation of the uterus with a catheter releasing irritant material into that area; a nonfatal rupture of the rectum due to carelessness in rectal examination or therapy; a perforation of the vaginal wall by the penis of the bull; an occasional severe hemorrhage, trauma, or rupture of the uterus at the time of calving due to torsion of the uterus, fetotomy, forced extraction, severe cervical or vaginal lacerations; a cesarean section; an extrauterine fetus; excessive bleeding following a manual removal of a corpus luteum; excessive massage or manipulation of an infected uterus such as rough removal of a retained placenta; and occasionally a parametritis due to a diffuse peritonitis secondary to tapping of the rumen or to traumatic gastritis. These

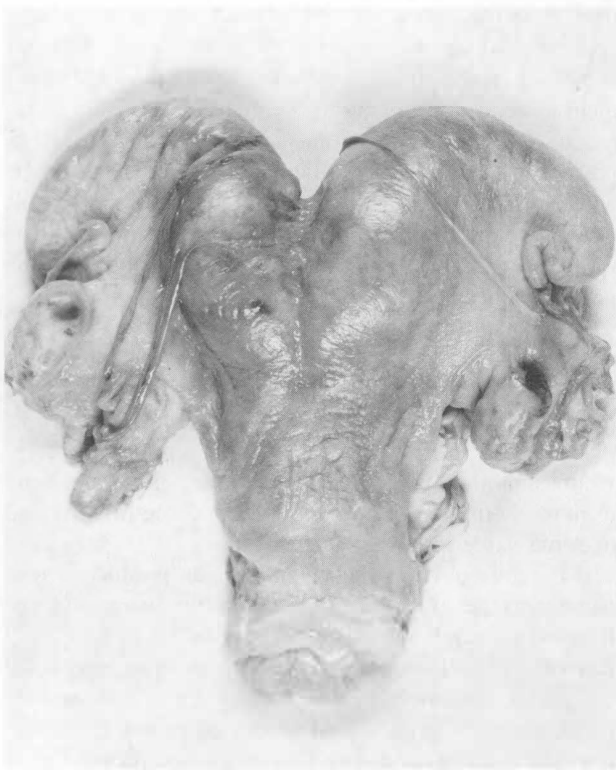


Figure 136. Extensive Perimetritis and Ovaritis with Adhesions Following a Severe Metritis after an 8-month-Abortion.



Figure 137. Abscess of the Uterine Wall Caused by the Improper Use of an AI Pipette.

conditions may be caused by tuberculosis of the genital organs in countries where tuberculosis in cattle is still common.

The lesions may vary from a few thin fibrous strands of connective tissue to firm adhesions between the uterus, broad ligaments, rumen, omentum, intestines, rectum, bladder, and other organs. The adhesions may be either diffuse or localized. In some cases abscesses may be found in the adhesions around the ovaries or broad ligaments or between the rectum and uterus. These localized abscesses may be either small or large. In rare cases one of these perimetrial abscesses may rupture into the rectum or bladder or may extend through the pelvic cavity to rupture alongside the vulva.

The symptoms of peritonitis in the pelvic region during the acute phase of the disease are the same as for any peritonitis: anorexia; arched back; slow, stiff gait; pain exhibited at the time of urination and defecation or at the time of a rectal examination; decreased rumen activity; and lack of ruminations. The temperature may be elevated for a day or two or may be normal. The pulse is elevated and the respirations increased. A "serous" or expiratory grunt may be heard at the onset of expiration or on percussion of the abdomen. The abdomen may be tense and the rumen slightly tympanitic. A diarrhea may be present. The hair coat may be rough. The drop in milk flow is usually marked. A hemogram may reveal

a slight leukocytosis and a shift to the left. A rectal examination in the acute case causes pain, tenesmus, grunting and an anxious expression. Fibrinous adhesions in this acute stage are usually easily broken down manually per rectum. If this condition is found, the rectal examination should be stopped immediately to prevent extension of the inflammatory process. If these acute symptoms are overlooked and the cow survives, the history will often reveal this period of illness. If death does not occur adhesions become chronic, areas of infection are walled off and become encapsulated abscesses that can readily be felt on rectal examination. Sometimes tumors or localized areas of fat necrosis may be confused with perimetritis and perimetrial abscesses. The prognosis in parametritis or perimetritis varies with the severity of the condition. Slight adhesions may cause no trouble, and sometimes can be broken by the hand in the rectum after the condition has become chronic. In severe, extensive adhesions the prognosis is poor to hopeless, especially if the ovaries and oviducts are involved in the adhesions or if the uterus is adhered to the abdominal organs over an extensive area. Such affected animals are usually sterile or fail to carry a pregnancy to term. In acute perimetritis conservative treatment with parenteral antibiotic and/or sulphonamide therapy is indicated.

Abscess of the Uterine Wall is occasionally observed



Figure 138. Ectropion of the External Cervical Os (three prolapsed transverse rings can be noted). (Courtesy K. McEntee.)



Figure 139. Lymphosarcoma of the Bovine Uterus. (Note the plaque-like thickenings of the uterine wall.)

in the cow. It is usually round or oval in shape and tense and firm on palpation. It may vary from 1 to 15 cm. in diameter, changing the normal outline or contour of the uterine horn. (See Figure 137.) It frequently occurs as a sequela to a severe metritis, rough or improper removal of a retained placenta, injury to the uterus due to improper or rough use of an inseminating pipette or other instrument and trauma especially to an infected uterus allowing infection to penetrate through the endometrium. Abscess of the uterine wall is easily palpated on rectal examination and should be differentiated from a tumor, cyst, or hematoma. Occasionally some perimetritis or adhesions may be felt around it. There are no general symptoms. In many instances the cow may fail to conceive. In several cases observed by the author the affected cows aborted at approximately 4 months of gestation on successive pregnancies and were sold as sterile. In another case the abscess ruptured into the uterus producing a pyometra. Treatment is usually impossible without the danger of causing a severe perimetritis or peritonitis. If the abscess is small the animal may recover but in many cases it is sterile. In rare instances adhesions form and the abscess may rupture into the rectum, bladder, or vagina. Parenteral antibiotic therapy might be indicated in early stages. Draining the abscess into the uterine lumen might be attempted as a last resort.



Figure 140. Adenocarcinoma of the Bovine Uterus.

Uterine Abscess is a condition similar to pyometra but characterized by a pathologic scarring or atresia of the cervix or vagina. It is usually due to severe trauma and necrosis caused by a dystocia or fetotomy operation. Cervical or vaginal atresia preventing the evacuation of the pus is very rare in the cow. If this condition is diagnosed the prognosis is usually hopeless and the cow is sold for slaughter.

Sclerotic Metritis is caused by a severe chronic metritis that has caused the complete destruction of the endometrium and fibrotic changes in the uterine wall. The endometrium is transformed into a thick, dense layer of connective tissue with foci of infection and purulent exudation into the uterine cavity. The uterus resembles a fistulous tract.⁴⁵ The condition often involves the cervix. This thickened indurated condition of the uterus usually follows a severe prolonged infection of the uterus such as chronic pyometra or fetal maceration. The uterine caruncles and endometrium are destroyed and the animal is therefore hopelessly sterile. The uterus on rectal examination feels very hard and firm, like cartilage or dense fibrous tissue. It is larger than normal and a chronic exudate may come from the uterus as well as from a thickened indurated cervix. In fetal maceration, bones may still be felt in the uterus. A sclerotic metritis should be carefully differentiated from an adenocarcinoma of the uterus which it may closely resemble. Usually the cow fails to show estrum and the corpus luteum is deeply

imbedded or retained. Slaughter is recommended.

Tumors of the Uterus in the cow are uncommon. In 6286 bovine genital tracts examined at slaughter there were 44 uterine tumors including 15 leiomyomas, 12 fibromyomas, 7 fibromas, 1 scirrhous adenocarcinoma, 1 lymphosarcoma, 1 spindle cell sarcoma, and 7 undiagnosed tumors.⁴⁰ In recent years a number of reports have indicated that lymphosarcoma and adenocarcinoma of the uterus are becoming more common.^{2, 11, 41, 46, 57, 63, 88} (See Figures 139 and 140.) The lymphoid tumor or malignant bovine lymphoma may involve the uterus and result in diffuse plague-like thickenings in the uterine wall. Affected cows may often be pregnant. The tumor is whitish-grey, compact and soft in consistency. Adenocarcinoma of the uterus is less common but this tumor may metastasize to other body organs and the peritoneum. In the uterus it feels hard, cartilaginous and umbilicated. It may ulcerate so that a bloody discharge comes from the cervix. Leiomyomas are usually single, firm, round and may resemble abscesses; they are benign. Careful rectal palpation of tumors of the uterus will differentiate them from abscesses, cysts, adhesions, tuberculosis and other uterine diseases.

Mucometra or Hydrometra is seen occasionally in cattle. Both mucometra and hydrometra are similar except for the degree of hydration of the mucin present in the uterus which may vary from a watery fluid to a semi-solid mass.⁴⁶ It has been described previously as a condition secondary to cystic ovaries and cystic endometrial hyperplasia usually associated with an anestrous period of 6 months or more. The ovarian cysts are usually small, 1 to 1.5 cm., two to four are usually present on each ovary. The cysts usually have a thick wall that resists rupture by manual pressure. The condition is further characterized by cystic degeneration of the endometrium and atrophy of the uterine wall, with an ounce to a gallon of thin to viscid mucus in the uterus. (See Figure 112.)

Mucometra is also observed in heifers or cows with arrests in the development of the Mullerian duct system or segmental aplasia of the paramesonephric ducts in which part of the vagina, cervix, or uterus may be missing or defective. (See Figures 120, 122, 126, 127.) Persistence of the hymen causing mucometra and muco-vagina has been previously described. (See Figure 124.) These genetic or congenital defects may result in a distention of both horns with watery, viscous, or even rather solid coagulated masses of mucus and cellular debris that may be confused with pregnancy. In these affected cattle the ovaries and endometrium are normal, and estrum therefore usually occurs normally. Rare cases of mucometra may be associated with retained corpora lutea.⁷⁶

In the cow, as in the dog, mucometra can apparently be produced by prolonged hormonal stimulation by estrogens and/or progesterone. The author has observed one case secondary to trauma and a fine adhesion obstructing the lumen of the cervix at the region of the internal os. In cases of mucometra no infection is usually present unless introduced accidentally by trauma, service, or treatment.

Cases of mucometra may be differentiated from pregnancy on a careful examination of the genital tract. Failure to slip fetal membranes, the presence of anomalies of the uterus, vagina, and cervix; the finding of ovaries that contain a single or multiple small cysts 0.5 to 0.75 inch in diameter; rarely the finding of a persistent corpus luteum on repeated examinations; the lack of enlargement or whirling of the uterine artery; the inability to palpate the fetus or cotyledons, although some cases with firm, gumlike-mucus in one horn or an apex of one horn may simulate a fetus or mummified fetus; the presence of a uterine wall that is usually thin and lacks tone when compared to the normal pregnant uterus; and the absence of regular developmental changes that occur in a normal pregnancy are the clinical findings on rectal examination of cattle affected with mucometra.

Cows with mucometra, or hydrometra due to defects of the genital tract are often sterile unless the case is a uterus unicornis and pregnancy occurs in the normal horn, or a simple imperforate hymen that can be opened. The advisability of using these cattle as breeding animals is questionable from an hereditary standpoint. In cows with mucometra and anestrus due to cystic ovaries, injection of a large dose of L.H., 20,000 IU of H.C.G. or more intravenously, or GnRH in large doses may occasionally bring about recovery. In rare cases of mucometra with a persistent corpus luteum an injection a luteolytic dose of prostaglandin F_{2a} or an analogue to involute the corpus luteum may be successful in correcting the condition.

Miscellaneous uterine diseases—A highly unusual **cystic placental mole** that follows embryonic death with the continued life and even growth of the membranes to a size corresponding to a 3 to 4 months' pregnancy together with retention of the corpus luteum has been described.⁴⁶ The mole has no lumen but consists of a mass of clear gelatin-like fluid. The "growth" may progress to pyometra or be expelled spontaneously. This condition should not be confused with the hydatidiform mole which appears as a grape-like cluster of translucent cysts or villi of the placenta and is expelled with the placenta. Chorioepithelioma in the cow is extremely rare.⁶³

Hyperkeratosis or X disease of cattle is caused by the ingestion of chlorinated naphthalenes formerly added to

oils and lubricants. It caused a marked lowering of the plasma vitamin A levels, a wrinkled, crusted, thickened skin, anorexia, depression, emaciation, abortion and even death. Retained placenta and metritis usually followed the abortion. In non-pregnant cows hyperkeratosis was characterized by metaplasia of the vaginal, cervical and uterine epithelium. Cystic enlargement of Gartner's ducts regularly developed.⁴⁷

Cervix

Cervicitis or inflammation of the cervix of the cow is commonly observed associated with metritis and frequently follows abnormal parturitions such as abortions, premature birth, dystocia, especially where forced extraction or fetotomy caused cervical lacerations or trauma, retained placenta, and postpartum metritis. Cervicitis especially of the external os of the cervix may follow injuries to the vulva and vagina allowing "windsucking" and vaginal contamination. Vaginal infections whether viral or bacterial usually produce a cervicitis of the external os. Occasionally a cervicitis may occur following trauma or puncture of the cervix by a catheter or insemination pipette. Care, patience, and gentleness should always be used in manipulating a catheter or pipette through the cervix. The cervix appears more resistant to infections than either the uterus or the vagina. The cervical infections are usually miscellaneous in nature and may be due to any of the organisms that infect the uterus or vagina. Certain organisms, such as *C. pyogenes*, are probably more pathogenic than others such as streptococci. It is possible that at coitus there may occur an introduction of infection that might cause some involvement of the external os of the cervix as well as the cranial portions of the vagina. The internal portions of the cervix appear rather resistant to the introduction of miscellaneous infections. Most cases of cervicitis originate at the time of or following parturition and often are associated with a metritis. Prolapse of the external transverse cervical rings or cervical ectropion is a possible factor causing cervicitis in older cows. (See Figure 138.) These prolapsed rings are often chronically thickened and fibrosed and circulation to the epithelium may be poor, permitting the establishment of infections. Severe purulent vaginitis or vaginitis associated with pneumovagina due to a lacerated or stretched vulva, atrophy of the perineal body and vulvar lips and horizontal tipping of the vulva may cause a severe cervicitis especially if urine and feces are present in the vagina. A poorly developed short cervix with very small transverse rings as described previously under genetic defects may readily permit an

endometritis to develop and a cervicitis may also be present.

Symptoms. Cervicitis can be diagnosed on vaginal examination with a speculum and light. The external os of the affected cervix is usually edematous and swollen, the external folds are often prolapsed, the cervical mucosa is a cherry-red to dark-purple color, and mucopurulent exudate may be seen in and on the cervix. There is little evidence that mild cervicitis without metritis prevents conception or causes sterility. Even when severe forms of cervicitis are present, conception may occur. Many clinicians have observed pregnant cattle with a mucopurulent vaginitis involving the external os of the cervix. The presence of a wide variety of bacteria, including streptococci and staphylococci, were demonstrated in the cervical mucus of 40 percent of postparturient cows. There was no evidence that the presence of these organisms had any effect on fertility.²⁶ Cervicitis was rather seldom a cause for sterility in the cases observed at autopsy.^{45,46} Since cervicitis and endometritis are closely associated and the former usually can be observed clinically, cervicitis may often be erroneously blamed for infertility. If a severe cervicitis is present endometritis or metritis may be present also and should be treated. Occasionally if pregnancy does occur even though a cervicitis is present the gestation may be insecure, with the possibility that abortion, retained placenta, and other uterine pathology may develop. Vigorous manipulation of the cervix will produce a marked hyperemia and congestion of the mucus membrane that should not be confused with infectious cervicitis. On rectal examination the infected cervix may be large and thick or may be normal in size. Hypertrophy of the cervix does not necessarily mean that cervicitis is present. Cervicitis does not occur commonly in the greatly hypertrophied cervixes noted especially in Brahman, Zebu and Santa Gertrudis cattle. Occasionally in severe chronic cervicitis the cervix may be very thick and sclerotic. The severity of the cervicitis will vary depending on the cause and length of time it has existed. The incidence of chronic cervicitis based on clinical examination was 0.6 percent.⁹⁴ It may be difficult to differentiate between cervicitis and metritis. If a metritis is present cervicitis is also present.

Cervical stenosis may follow severe infection or trauma. Cervical atresia or obstruction is very rare in the cow. If it occurs the mucus and exudate remain in the uterus, and the uterus becomes distended. Depending on the nature of the uterine contents a uterine abscess or mucometra develops. Cervical stenosis may occur due to severe cervical inflammation, or an enlarged cervical ring may extend into the cervical canal, making a sharp bend in the lumen so that passage of a catheter is difficult or

impossible. These cows frequently conceive promptly when bred naturally or when semen is deposited artificially in the cervix. In rare instances described previously, a severe sclerotic, fibrosed, indurated cervix may result in cervical stenosis at the time of calving causing dystocia. In occasional cases following a dystocia a necrotic cervicitis or a severely lacerated cervix may be present producing a severe scarring of the mucous membrane.

Prognosis—The prognosis in most cases of cervicitis is good and spontaneous recovery usually occurs as the metritis and vaginitis improve. As long as a metritis or severe vaginitis is present, recovery from a cervicitis cannot occur. The cervical infection usually is overcome by the natural body-defense mechanisms particularly if the estrous periods are regular. The more severe forms of cervicitis may take longer to respond. Cervical stenosis or sclerosis frequently fail to respond to treatment, and if the cow conceives these conditions are apt to cause dystocia at the time of the next parturition. Cervical ectropion, or prolapse of the external cervical folds, does not improve. Usually the prolapsed transverse rings become a more ectropic with each calving.

Treatment—If metritis or vaginitis accompanies the cervicitis then the entire reproductive tract must be treated. The same treatments usually are useful for all 3 conditions. It should be recognized that ordinarily the cow overcomes cervicitis spontaneously, as it does other infections of the genital tract. The following treatments may aid and hasten recovery. Warm or hot mild antiseptic douches of the vagina every 3 to 4 days as described for endometritis are useful in flushing out the mucopurulent exudate and stimulating circulation in the mucosa of the vagina, cervix and uterus. Douching the cervix and uterus may also be useful. Many veterinarians prefer to swab the cervix with one of the following: Lugol's solution; a cervicitis mixture such as (A) phenol 1 part, tincture of iodine 1 part and glycerine 2 parts, or (B) menthol crystals 1 dram, tincture of iodine 4 ounces and glycerine 4 ounces. The cervix is swabbed by pulling it back toward the vulva with cervical forceps and then with gauze wrapped around a long pair of dressing forceps soaked in Lugol's or cervicitis mixture the entire length of the cervix is thoroughly swabbed. Although this treatment probably does not completely eliminate infection it stimulates mucous flow, causes hyperemia, and apparently hastens recovery. The use of stronger preparations such as 10- to 20-percent silver nitrate solutions are not indicated as they may cause too much damage and may result in cervical adhesions. Some veterinarians inject antibiotic or sulfonamide solutions and preparations into the cervix and uterus and expect that as it is

expelled the material will help overcome the infection in the cervix. Some prefer to rub or infuse a sulfonamide or antibiotic ointment or 1 percent acriflavine ointment into the cervical lumen. If cervicitis is secondary to vaginitis and pneumovagina, a vulva-suturing operation should be performed as described under the treatment of vaginitis.

In certain cases of chronic cervicitis of the external os associated with severely prolapsed cervical rings that fail to respond to treatment, the external cervical rings may be amputated. This may be done readily with large serrated scissors. After the prolapsed rings have been amputated the vaginal mucosa may be sutured to the cervical mucosa to help control hemorrhage and promote rapid healing but this is not necessary.³³ Epidural anesthesia is not required as there are no sensory nerves in the cervix but it aids by controlling defecation during the operation. Trachelorrhaphy is the suturing of cervical lacerations after calving. Partial trachelectomy is the amputation of a portion of the cervix. This operation is probably not necessary since cervical infections of the external os seldom prevent conception and the internal portion of the cervix provides a firm seal even though the external os may be ectopic and inflamed. Usually within 3 to 4 weeks after amputation of the prolapsed cervical rings healing has occurred and breeding can take place. Regular estrous periods have as definite a healing

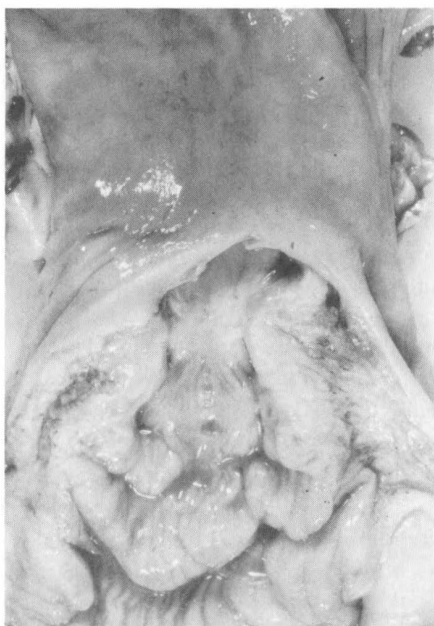


Figure 141. Atresia of the Internal Os of the Cervix Secondary to an Acute Cervicitis (Mucometra resulted).

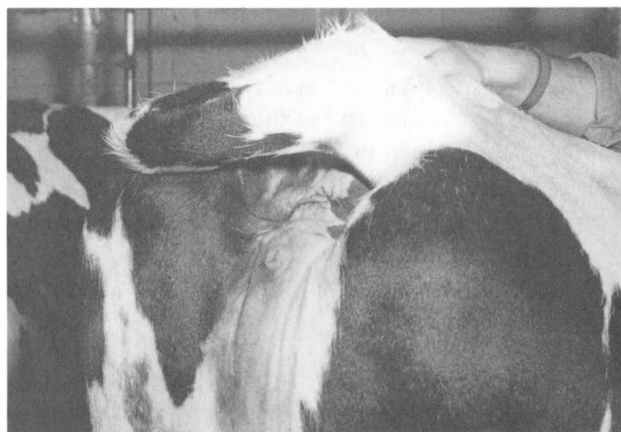


Figure 142. A Horizontally-tipped Abnormal Vulva Causing Pneumovagina in a Cow. (Suturing of the vulvar lips was followed by conception in this "repeat breeding" cow.)

effect on cervicitis as they have on endometritis. If cervicitis is severe, sexual rest is indicated for two or more estrous periods. Manual or instrumental dilation of an atretic or stenosed cervical canal is useless. The bovine cervix usually ruptures before a significant dilation occurs.

Cervicitis may be prevented by the same precautions that can be taken to prevent endometritis or vaginitis. Trauma to the cervix should be avoided whenever possible.

Cysts of the Cervix are observed occasionally in the cow. These are sometimes called "Nabothian" cysts or follicles, after the terminology used for this condition in humans. These cysts vary in size from 1 to 5 cm. in diameter. They are apparently retention cysts of the cervical glands. They may be congenital but are usually acquired secondary to trauma or lacerations. Frequently they go unnoticed until they become large and palpable as a fluctuating mass in the cervix on rectal examination. Often a portion of the cyst may be observed in the external os on vaginal examination. These cysts apparently seldom cause infertility but they might be large enough to hold some mucus and debris in the uterus, prevent proper closure of the uterus by the cervical seal during pregnancy or possibly interfere with the passage of spermatozoa. They are easily treated by incising with a needle, teat bistoury, or small knife through the external os of the cervix. Following incision and draining of the mucus from the cyst, the cervix may be swabbed with Lugol's solution or other cervicitis mixture. In some cases a cyst may require differentiation from an abscess; it is usually thin-walled and covered only by mucous membrane whereas the abscess is deeper in the tissues of the cervix

and has a thicker, more fibrous wall of connective tissue. Cysts of the cervix should also be differentiated from occasional cystic dilations, sacculations, or diverticula of the cervical lumen in cattle due to arrests in the development or fusion or developmental defects of the Mullerian ducts. These may be genetic or congenital in nature (See hereditary defects of the cervix). The prognosis is usually guarded to poor.

Complete Stenosis or Obstruction of the Cervix, except secondary to trauma or severe inflammation, is probably very rare in the cow. In some heifers with a small or tortuous cervical canal an insemination pipette cannot readily be passed. If these animals fail to conceive the stenotic cervix may be considered to be the cause. In 1711 heifers and 11,112 cows the cervix was impenetrable to an inseminating pipette in 11.7 and 1.1 percent of the cattle, respectively.⁶⁹ When semen was inseminated into the cervix the conception rate in the affected heifers was 54.0 percent, and in the cows 36.5 percent, indicating that this condition should not be considered abnormal and a cause of infertility. The author and his associates have observed only one case of cervical atresia in the cow not associated with an anomalous condition, and this showed evidence of previous trauma. (See Figure 141.) If the cervix were actually obstructed the uterus should fill with mucus and other cellular debris similar to that observed in cattle with certain congenital defects of the reproductive tract, such as seg-

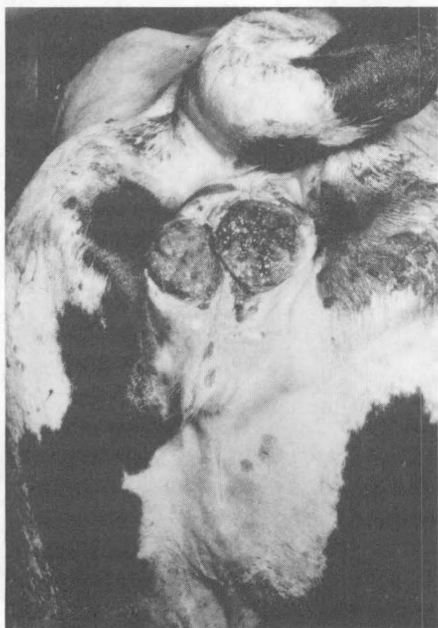


Figure 143. Carcinomas of the Vulva of a Cow.



Figure 144. An Anomaly or Wattle, Present on the Vulva of a Heifer. (Courtesy K. McEntee.)

mental aplasia of the Mullerian ducts or an imperforate hymen. In heifers with an infantile, abnormal, or stenotic cervix, treatment as described under hereditary defects of the cervix should be followed.

Mucocervix—In rare instances the cervix may be greatly enlarged to about 10 to 15 cm in diameter and 15 cm in length with an enormous pathological cervical seal of tough tenacious mucus. This condition is probably a hormonal disturbance due to a deficiency of L.H. or GnRH. It is usually associated with a failure of estrus with chronic cystic ovaries or a retained corpus luteum. The prognosis is usually very poor. The intravenous or intramuscular injection of a very large dose of L.H. or GnRH or possibly prostaglandin may be helpful in the treatment of these cases. An anomaly or defect of the cervix usually fills with mucus.

Tumors of the Bovine Cervix are rare. Fibromas, fibrosarcomas, leiomyomas, and carcinomas affecting the cervix have been described.^{11,63,88,90} Most of these tumors were benign. In rare instances adenocarcinomas may be malignant and metastasize to other organs.

Vagina

Vaginitis in the cow is observed as a primary or secondary condition. The secondary condition is often as-

sociated with metritis and cervicitis. Vaginitis may occur following trauma, lacerations, and bacterial, viral or protozoal infections produced or introduced at the time of service, abortion, dystocia, fetotomy, retained placenta, prolapse of the vagina, and postpartum metritis. Severe stretching or laceration of the vulva especially of the perineal body, and in older cows sinking of the anus and tipping of the vulva into a horizontal position, with an atrophy of the vulvar lips often results in pneumovagina and contamination of the vagina by feces, urine (urovagina), air, and miscellaneous debris and infection that often cannot be readily expelled because the uterus and cervix have pulled the cranial portion of the vagina forward and downward into the abdominal cavity (See Figure 142). A vaginitis may occur following coitus, especially in heifers bred to an old bull, but this is usually a mild and transient condition. Occasionally small abscesses may develop in the mucosa or in Gartner's ducts. In rare instances vaginitis may be due to treatment of the vagina with irritant preparations, introduction of infection on instruments, or examination of the vagina in a dirty, unsanitary manner. Most vaginitis is due to non-specific infections such as staphylococci, streptococci, coliform organisms, *C. pyogenes*, urea- and mycoplasmas and others. The vaginitis due to specific infections such as **IBR-IPV**, "epivag," and possibly other viral infections, trichomoniasis, vibriosis and granular venereal disease has already been discussed. Necrotic vaginitis and severe vaginal lacerations following calving, dystocia, and fetotomy have been discussed previously in Chapter XI.

Symptoms of Vaginitis—In the cow a mucopurulent, yellow-grey pus is usually discharged from the vulva at irregular intervals and mats the hair of the vulva, tail and buttocks. On vaginal examination the exudate is observed on the floor of the vagina and the vaginal walls are congested, edematous, and inflamed. The more severe the inflammation the more red and inflamed the vagina. In some cases ulceration of the mucosa, lacerations and secondary diphtheritic or necrotic lesions occur especially around the vestibulo-vaginal border and in the vestibule and vulva. In severe cases the cow may show tenesmus, irritation, and pain probably due to the concurrent vestibulitis and vulvitis.

If the vulva is stretched, damaged, torn, or deformed, so that pneumovagina results, the vagina may then contain fecal material, urine, and air as well as mucopurulent exudate. (See Figure 142.) This may frequently be a cause of failure of conception, particularly in older cows in the large breeds, such as Holsteins, Brown Swiss, Herefords, Santa Gertrudis, possibly Brahmas, and occasionally Guernseys. Under most circumstances an un-

complicated mild vaginitis may not prevent conception. Since vaginitis can be associated with cervicitis and endometritis it is probably the latter condition that in most cases causes the infertility, although a severely diseased vagina and external os of the cervix filled with pus and debris and having an altered pH may cause rapid destruction of spermatozoa and interfere with fertilization. In pneumovagina in old cows or **Bos indicus** breeds with a large heavy cervix pulling the vagina forward and downward, an accumulation of material in the vagina, often associated with an atonic uterus hanging low in the abdominal cavity, may cause some infectious material to pass through the infected and relaxed cervix and thereby cause an endometritis. Often in these older cows with the characteristically deformed perineum, the vulvar lips may be parted with the fingers and air will rush into the vagina. In 20 cases of infertility apparently due to pneumovagina treated by the author, the cows had been bred unsuccessfully 2 to 8 times, or an average of 4.5 times. After correcting the condition, 18 (or 90 percent) conceived within 21 to 60 days. Although this is too small a number upon which to base a definite conclusion the fact nevertheless remains that following the closure of the vulva the vaginitis cleared up very rapidly and conception occurred similar to the condition in mares. From what is known concerning the value of the operation in mares the author feels that this procedure has received too little attention in the treatment of sterility in cattle. The external os of the cervix is usually involved in any vaginitis. If metritis or cervicitis is present some of the vaginal discharge may actually come from those sites and the vagina is involved secondarily. Necrotic vaginitis, as described previously following a difficult parturition, may also follow the accidental use of caustic agents as in a douche. In rare cases secondary stenosis and even atresia of the vagina may follow a severe vaginitis. In urovagina it may be necessary to surgically create a fold or dam of the vaginal floor to prevent urine from entering the vagina.

The Prognosis in simple vaginitis due to the causes listed above is good, and most cases will respond spontaneously even without treatment unless pneumovagina is present or unless a severe chronic cervicitis or metritis is also present. The prognosis is poor if stenosis or atresia of the vagina is severe. If the vaginitis is caused by an infectious agent, local antibodies are usually produced that aid in the elimination of infections such as **C. fetus**, **Tr. fetus** and **IBR-IPV**.

The Treatment of vaginitis usually consists of mild aqueous douches of 200 ppm chlorine solution, antiseptic aromatic soap solutions, dilute potassium permanganate solutions, 1:1000 to 1:3000 acriflavine solu-

tions, 200 ppm quaternary ammonium compound solutions, sodium bicarbonate solutions, solutions of chlorhexidine, or betadine and saline solutions. Irritating douches are unnecessary and should be avoided. Usually 2000 or 4000 ml of a solution are used and introduced either by means of a catheter and funnel, an enema bag and tube, or by holding the extended hand palm upwards in the vestibule pinching down the cow's back, and pouring the solution over the palm of the hand into the vagina. This flushing of the vagina may be repeated several times to wash out mucopurulent material. Retreating may be helpful at daily or 3- to 4-day intervals. Besides douching, some veterinarians introduce sulfonamides or antibacterials such as: penicillin, streptomycin, neomycin, furacin, tetracyclines or others in an ointment form or in oil-and-water emulsions. Others infuse the vagina with bland antiseptics in oil, such as sulfonamides and bismuth formic iodide, 1 ounce in a pint of oil, or iodine in oil; this may be repeated twice a week. If a cervicitis or metritis is present these should be treated also.

In cases of pneumovagina the vagina is usually douched thoroughly, an antibiotic solution or preparation is placed in the uterus, cervix, and vagina. Then under epidural anesthesia of the vulvar lips, as in the Caslick operation in the mare, the mucosa of the outer 1 to 1.5 cm. of the vulvar lips is scarified from the dorsal commissure to the level of the ischial arch. Often only a 2.5 to 3 cm. ventral vulvar opening is left after suturing. Sutures should be of chromic catgut or nylon. Since the cow's tail rests and rubs on her vulva, clips are not satisfactory as they usually are rubbed out. The interrupted sutures should be about 1 cm. apart and not put in so tightly that the suture cuts the tissues. The sutures may be removed in 7 to 10 days. (See Figure 85.) The vulvar opening after this operation is small and service by artificial insemination usually is necessary. During the last week or two of gestation the vulva should be incised along the original suture line so that no tearing of the vulva will occur at parturition. The vulva needs to be resutured after calving. In certain cases the removal of a large elephant ear-shaped sections of perineal skin between the anus and vulva and the ischial tuberosities results in drawing the anus caudally when these lateral wounds are closed. This "plastic" surgery aids in restoring a normal vulvar configuration. Occasionally an area of skin below the ventral vulva commissure may be removed to draw the latter structure ventrally.⁹

Urine pooling in the vagina may rarely occur associated with pneumovagina, as in the mare, and in bilateral sacroiliac luxation. A simple, successful technique to correct urovagina and restore fertility has been described.^{35b} It consists of constructing a transverse fold or

dam about 5 to 7 cm. high in the caudal floor of the vagina cranial to the urethral orifice by a continuous horizontal mattress nylon suture that is left in place for 30 days to make the dam permanent by the development of scar tissue.

Cysts of the Vagina are not uncommon. Cysts of the mesonephric or Gartner's ducts in the floor of the vagina are usually small, 1 cm. wide and 1 to 3 cm. long. There may be several cysts along the course of the ducts. (See Figure 129.) These cause little harm and usually they are not found except on speculum or manual examination of the vagina. They are seldom treated. Gartner's duct cysts are described under congenital defects since these ducts are remnants of the Wolffian or mesonephric ducts. In rare instances these cysts may become infected. On rare occasions single cysts up to 3 cm. in diameter, not of mesonephric duct origin, may be seen in the mucosa of the cranial and dorsal or lateral portion of the vagina.

Tumors of the Bovine Vagina have been described and include: fibromas, fibrosarcomas, leiomyomas, hemangiomas, lymphosarcomas, and carcinomas.^{11,63,88,90,92} Vaginal tumors are unusual in the cow. They seldom cause infertility but may cause dystocia, as do those of the cervix, if they are large enough. Most of the tumors are benign and pedunculated. Occasionally they may protrude through the vulva and surgical removal may be necessary. Excessive bleeding may occur unless steps to control it are taken at the time of the removal of the tumor.

Vestibule and Vulva

Vestibulitis and Vulvitis are similar to and treated in the same manner as vaginitis. Most cases of vulvitis are characterized by granular venereal disease lesions. Severe inflammations of the vulva may cause straining, refusal to copulate, and pain on examination. In severe cases the vulva is usually swollen and a mucopurulent discharge such as in severe granular venereal disease due to ureaplasma or other organisms or IBR-IPV infection, is present. Severe injury and lacerations of the vulva or vestibule caused by tearing of the vulva at the time of parturition, or by horn wounds should be sutured at once to prevent pneumovagina. Necrotic vulvitis and vestibulitis may follow severe trauma, ischemia and infections such as *S. necrophorus*. An outbreak of necrotic vulvitis affecting 170 Hereford feedlot heifers was reported.⁶⁶ This was a localized necrosis of the vulva that varied in size from a small area of sloughing to one involving nearly the entire vulva. The heifers did not become clinically ill and recovered in 3 to 5 weeks. The cause of the condition was not known but a virulent *S.*

necrophorus infection or an allergic type of reaction was suspected. Edema of the vulva and perineal region in clinical allergies or urticaria is common.⁸

Cystic Vestibular (or Bartholin's) Glands are often observed in the lateral wall of the vestibule. They arise from an atresia or obstruction of the duct of the gland that usually opens on the lateral wall of the vestibule at the vulva-vaginal border. This small paired gland secretes a rather clear mucus. Obstruction of the duct opening is usually due to trauma or severe inflammation, such as a local necrotic vaginitis, at the time of calving. This gland may enlarge due to the accumulation of fluid, until it is 2 to 10 cm. in diameter. When the cystic gland becomes larger than 5 cm. in diameter it usually shows between the vulvar lips when the cow is lying down as a round pink mucosa-covered object that is often mistaken for the beginning of a prolapse of the vagina. The cystic vestibular gland is almost invariably unilateral in occurrence and is seen in older cows and only rarely in heifers. It causes no problems at parturition nor does it interfere with conception. Occasionally when it is large it protrudes through the vulvar lips and becomes covered with feces and dirt. When the cow rises and the cyst returns to the pelvic canal contamination of the vestibule, vulva and caudal part of the vagina may occur. These cysts are easily handled by making a liberal incision therein. Painting the opened cyst with Lugol's solution, although commonly done, is probably not necessary.

The Tumors of the Vulva include: fibromas, fibrosarcomas, angiomas, carcinomas and fibropapillomas.^{11,44,46,63,88,90,92} A report on 28 fibropapillomas from the vulva and vagina of cows and 27 from the penis of bulls concluded that, because these occur primarily in young cattle usually in several animals on the same premises, the fibropapilloma is a transmissible tumor of the external genital organs of cattle.⁴⁴ This tumor undergoes spontaneous regression in about one to 6 months. It is similar to or the same as the common wart or papilloma found on the body skin of young cattle and caused by a virus.⁴⁴ The prognosis on squamous-cell carcinomas of the vulva are guarded to poor as often the regional lymph nodes may be affected. Slaughter is usually advisable. A small finger-like wattle is rarely observed on the vulvar labia (See Fig. 144).

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THE REPEAT BREEDER COW

The discussion of this important infertility condition has been intentionally left to the end of this chapter because most of the diseases previously described are causes of failure of conception. The repeat breeding cow is one that has normal or nearly normal estrous cycles and estrous periods and has been bred 2 or 3 or more times to a fertile full or with fertile semen yet failed to conceive. The clinical examination of the animal may fail to reveal any definite lesion or condition to explain the failure of conception. The major proportions of the problem have been outlined but limited advances have been made in studying some of the various causes and still less on the diagnosis of causes in the individual cow. The greatest advance in this problem of "repeat breeders" has been the demonstration of the role of vibriosis in early embryonic deaths. It is unfortunate that many of the experiments performed before the mid 1950's and cited below did not consider this important cause of infertility.

In recent years the problem of repeat breeders and infertility in cattle has been reviewed.^{3,17,49,71,100} Infertility and breeding efficiency in a large dairy herd over a period of 30 years that included 2607 cows and nearly 10,000 breeding periods was reported upon.²⁸ The most common causes for infertility in which the fetus was carried to term were: short cycles, 24.2 percent; cystic follicles, 11.3 percent; and infection of the genital tract, 15.1 percent. The conception rate on services carried to term in clinically normal cows was 51.9 percent. In a recent report on 9750 Holstein cows in 125 herds in New York

State the conception rate on first, second and third services were 50, 51 and 53 percent with total conception rate after two and three services of 76 and 89 percent, respectively.^{79b} The various causes of repeat breeding have been classified differently by investigators. Some workers in the field of reproductive physiology have divided the causes into two groups: (1) failure of fertilization and (2) early embryonic death.¹⁷ Others,^{99,100} including the author, prefer a more detailed classification based on pathological and managerial causes namely: 1. congenital or genetic anatomical defects of genital tract, 2. congenital, genetic or acquired defects of the ova, spermatozoa or early zygote, 3. infectious or traumatic inflammatory processes, 4. endocrine disfunctions, 5. managerial and nutritional deficiencies. Modern herds incorporating large numbers of cattle and employing artificial insemination have many problems in heat detection, timing of service, and in the care and handling of semen in which the herdsmen and inseminators can influence the incidence of infertility and repeat breeding. Because of the multiplicity of causes for repeat breeding that varies from herd to herd, cow to cow, and estrus to estrus, diagnosis and therapy by the veterinarian requires great diagnostic skill and knowledge.

A survey of the problem of repeat breeding has shown the overall incidence in two large studies to be about 10 percent (9.1 to 11.1) to 15.1 percent (6.7 to 20.9), respectively.^{44,99} Over 50 percent of the farms surveyed had this average incidence of affected animals. As the herd size increased so did the incidence of repeat breeders. In New York State herds with over 90 cows had 5 to 10 percent lower conception rates than herds with about 50 cows.^{79a} The highest seasonal incidence of repeat breeders was in the fall and winter months with the lowest incidence in the spring and summer months, 10.2 to 13.7 and 7.1 to 9.4 percent, respectively.⁴⁴ The incidence of repeat breeders is lowest in heifers that had calved for the first time, 5.2 percent and then in older cattle it rose and in 9-year-old or older cows it was 13.3 percent. In another large study dairy cows over 7 years of age had a 15 percent lower conception rate than cows under 3 years of age.^{79a} The calving interval also increased. There was a marked tendency for cows to revert to spring calving with increasing age. Repeat breeding was also more common in cows with higher milk production. Only 10 percent of the herds or individual cows affected with an infertility or repeat breeding problem one year continued to be affected the following year.⁷¹ The herds with infertility problems remained constant at 6.5 percent from year to year in Kentucky. A study of records on 75,000 cows in the Netherlands also showed fertility decreased as animals grew older, from 68 to 58

percent in virgin heifers to cows with their tenth calf.⁹¹ As herd size increased there was a decrease in fertility. The greatest fertility was on farms raising grade cattle.

A summary of five of the early classical experiments on repeat breeding cows and heifers was prepared.⁶⁹ Most were taken from herds artificially inseminated. The animals were examined clinically and those with obvious disease of the reproductive organs and over 10 years of age were eliminated. However, in these early studies **C. fetus** might have been an important cause for infertility. Not more than 2 cows were taken from any one herd. The cows were bred to a fertile bull by artificial insemination on the second estrum after arriving at the central location for the experiment. One-half of these were killed on the third day after breeding and the oviducts were flushed to recover the ova, which were then examined to see if fertilization had taken place. Fertilization was noted by cell division in the ovum. The other half of the animals were scheduled to be killed at 34 days after insemination. If they came back in estrus before this time they were rebred and killed the third day. At the time of slaughter on 34 days the presence or absence of a normal, living embryo was noted. Thus from the findings at these 2 times the percentages of fertilization and of early embryonic deaths were determined. In these five studies 313 ova were recovered with a **fertilization rate** of 65.5 percent.⁶⁹

In two later studies, the fertilization rate of 120 recovered ova in 97 normal virgin heifers was 85.5 percent.^{9,10,52} Fifty one heifers bred to highly fertile AI bulls (70 to 79 percent conception based on 60 to 90 day nonreturns), had a fertilization rate of 96.1 percent; while 46 heifers bred to AI bulls with low fertility (40 to 60 percent conceptions based on nonreturns at 60 to 90 days), had a fertilization rate of only 76.1 percent. In 299 repeat breeding cattle, 6.4 percent failed to ovulate, 5.4 percent had occluded oviducts and 4.7 percent had abnormal or defective ova which accounts for some definite causes of failure of fertilization.⁶⁹ There was no apparent cause for failure of fertilization in over 23 percent of the repeat breeding cows. Low fertility of semen and possibly improper timing of service might have accounted for some of this failure of fertilization due to no apparent cause. Using highly fertile sires for breeding cows, especially repeat breeders, is highly desirable.

An incidence of 28.5 percent **early embryonic deaths** was reported in 199 repeat breeder cows.⁶⁹ As mentioned before it was unfortunate that the status of these animals with regard to **C. fetus** infection was not ascertained. When 26 virgin heifers were inseminated with antibiotic-treated semen from bulls of low fertility and 29 virgin heifers with semen of high fertility; the percent of nor-

mal embryos present at 33 days in the two groups were 57.7 and 86.1, respectively, with an estimated embryonic death rate of 19.6 and 10.5 percent respectively. This latter difference was not statistically significant.^{9,10}

Embryonic losses were similar in another study in heifers inseminated with spermatozoa from bulls with a high and low fertility.⁵² Although the quality of semen will influence both fertilization and embryonic death rates the results are not consistent.³ The average incidence of embryonic death in virgin heifers was 15 percent.⁷¹ The evidence indicated that repeat breeding, when highly fertile bulls were used, was largely due to embryonic deaths; while in repeat breeders bred to bulls of low fertility both failure of fertilization and early embryonic deaths occur. Most embryonic deaths occur soon after 16 days of gestation.⁴ In a study of 183 normal and repeat breeding cows in Israel by slaughter at gestation days 3, 11 to 13, 14 to 16, 17 to 19, and 35 to 42, the following percentages of viable embryos in the normal and repeat breeder groups were found 83 and 71, 89 and 50, 47 and 43, and 69 and 35, respectively. The fertilization rates were about the same in the two groups and most embryonic deaths occurred from 11 to 42 days.⁴ Most early embryonic death loss that was going to occur by 26 days had already occurred by 12 days of gestation.¹³ A 15 percent failure of fertilization, a 7.5 percent early embryonic death loss by 26 days, and an 8.0 percent further loss of older embryos and fetuses later in gestation was reported in 112 fertile Ayrshire cows inseminated with fertile semen.¹³ In a recent study of 3 groups of 47, 51 and 57 virgin Brahman heifers slaughtered on days 3, 16 and 35 postinsemination, respectively, the conceptus was recovered. At 3 days the fertilization rate was 80 percent. The percent of viable embryos at 16 and 35 days were 78 and 72, respectively. Thus most early embryonic loss occurred by day 16.^{79b} Embryonic deaths occurring at 8 to 16 days after breeding usually do not affect the normal cycle length of about 18 to 24 days but embryonic deaths occurring at 16 to 25 days often result in longer periods between service and the next estrus.

Embryonic mortality was monitored by milk progesterone assays in two studies through 75 days of gestation in dairy cows in the U.S. and England. In the former study,⁵⁴ 153 cows had continuous high progesterone levels for 28 or more days after insemination. Of these, cycling was reinitiated in 11 cows or a 7.2 percent embryonic mortality. This was considerably less than the estimated rate of 22.7 percent based on delayed returns to estrus. In the latter study⁶ 200 cows were monitored from 17 to 70 days after insemination for two years with an embryonic death rate of 9.7 percent after elimination of 6 cases caused by insemination at a false heat during

pregnancy. The incidence of embryonic deaths ranged from 3.3 percent in primipara to 15.1 percent in cows after their third lactation. Most embryonic deaths occurred around 35 days of gestation. The exact interval from embryonic death and return to estrus with a decline in progesterone is not known. However it has been reported abortion and estrus occurs 14 to 35 days after physical destruction of the embryo or early fetus by rectal manipulation from 30 to 90 days of gestation.⁵ Estrus and embryo or fetal expulsion occurred within 5 days when the CL was removed manually.

Certain bulls have a higher fertilization rate than other bulls. In one study of 12 beef bulls the pregnancy rate following natural service for 9 bulls ranged from 61 to 80% with the other 3 bulls having pregnancy rates of 0, 12 and 95%. With the exception of the sterile bull with no conceptions, breeding soundness examinations before and after the trial, scrotal circumference and semen quality had low correlations with bull fertility in this and also other cited studies.^{56b} Also heterospermic insemination, the insemination of a female with a mixture of semen from more than one male has been reported to improve fertility over homospermic insemination, which utilizes semen from only one male. In one study⁶⁸ no increase in fertility occurred when a semen mixture from two bulls was compared with homospermic insemination but when semen from 3 bulls was mixed, conception rate was significantly higher, 70.6 percent vs. 62.7 and 62.2 percent from homospermic inseminations or the seminal mixtures from 2 bulls. Heterospermic inseminations with frozen semen mixture from 3 bulls produced a definite deviation from the expected equal number of progeny per sire with one bull siring 47.2% of the calves. Pregnancy rate to one natural service did not differ from that of multiple services by a single sire. However multiple sire matings by 3 sires increased pregnancy rate per estrus by 10 percent, 73 to 63 percent, over that by single sire matings, respectively. This difference, as well as those in studies using heterospermic semen from 2 or 3 sires artificially, was simply a reflection of the degree of fertility of the single sire, or the most fertile sire in the multiple sire matings.^{56b}

In an excellent review of the problem of early embryonic deaths a large part was due to genetic causes as evidenced by the unexplained differences in fertility between males and the decline in fertility associated with age.¹¹ Thus much of the embryonic death rate is unavoidable and should be regarded as a normal way of eliminating unfit genotypes in each generation at a low biological cost. Thus, if one accepts the reported conception and pregnancy rate in cattle of 60 percent or 1.6 services per conception, and breeds 100 hypothetically

normal cows, 60 will conceive on the first service, and 9.6 of the remaining 16 will conceive on the third service.²¹ Thus in this hypothetical example using normal cows and bulls 6.4 percent of the cattle will require 4 or more services. Thus a certain percentage of repeat breeders are normal fertile cows.

The possible causes for fertilization failure and early embryonic deaths will be considered in the following classification based on pathological or managerial causes for infertility and repeat breeding.

Pathological Causes for Repeat Breeders

Genetic or congenital anatomical defects of the genital tract—These defects include principally the anomalies or segmental aplasia of: the uterine tube which is rare, the uterus, the cervix, and the vagina as have been described earlier in this chapter. These defects and anomalies largely cause failure of fertilization (F.F.) by preventing the union of the sperm cell and the ovum. Bilateral defects usually result in complete sterility. In some conditions, such as a lack of a normal endometrium, fertilized ova could not survive and form attachments or in underdeveloped cervixes proper protection for the uterus is not provided so endometritis and embryonic deaths (E.D.) result. All of these defects are present in heifers at the time of puberty but in the less severe conditions, such as uterus unicornis, repeat breeding may occur but conception and a normal pregnancy may follow and the condition may not be diagnosed until the second or subsequent breeding period. The genetic or congenital anomalies of the genital canal are infrequent causes for repeat breeding and many can be diagnosed by a careful rectal and vaginal examination. Genetic or hereditary defects causing infertility or sterility and possible chromosomal abnormalities in cattle were discussed earlier in this chapter.

Genetic, Congenital or Acquired Defects of the Ova, Spermatozoa or Early Zygote—A low incidence of about 5 percent of grossly abnormal ova were observed in repeat breeding cows,⁶⁹ and 2 percent in normal heifers.^{9,10} The possibility of a greater number of ova with defective chromosomes seems likely from reports cited previously to indicate a higher incidence of infertility in Guernseys and Brahman cattle kept on the same premises and under similar conditions as other more fertile breeds. The lowered fertility of older cows may well be related in part to defective ova. In a study of 37 blastocysts from 23 repeat breeding heifers only 30 percent were normal. While examination of 31 blastocysts from 18 normal virgin heifers 74 percent were normal—a highly

significant difference between the two populations.⁵⁶ Postovulatory aging of mammalian ova often resulted in failure of fertilization or polyspermy and early embryonic deaths.^{55,69,70} This may occur by breeding cows too late following the end of estrus. Inbreeding of the zygote and the dam has a deleterious effect on the conception rate and embryonic survival.^{17,18,57} If intensive inbreeding is followed, certain lines may experience marked infertility. Daughters of certain bulls are apparently more fertile than daughters of other bulls. This may partly be a reflection of the chromosomal constitution of the ova.^{31,48} Superior reproductive performance is usually reported in cross-bred cattle.⁵⁹ Thus heterosis can dilute or render ineffective lethal genes possibly present in purebred or closely bred lines.

A chromosome translocation, 1/29, in the Swedish Red and White Breed was reported in which 14 percent were heterozygotes and 0.34 percent were homozygotes for the translocation.³⁴ Daughters of translocation sires returned to service more often than daughters of normal sires apparently due to an increased embryonic death rate. About 10 percent of embryos from apparently normal gilts had chromosomal abnormalities, mostly trisomies, that were probably incompatible with life.^{60,61} In the future probably more genetic chromosomal anomalies causing infertility will be found.

The literature concerning the deleterious effects of aging of the ova after ovulation and aging of the spermatozoa before and after ejaculation into the female has been reviewed.⁵⁵ Gross anatomic genetic defects of the male reproductive tract resulting in oligospermia and aspermia due to anomalies of the mesonephric duct system have been described and result in infertility or sterility in the bull. Many genetic or congenital microscopic defects in spermatozoan morphology and chromosomes that prevent fertilization or result in infertility in bulls have also been described in Chapter XVIII. Some of these affected bulls may have a nearly normal semen picture. Other sperm cell abnormalities such as atypical basic nuclear protein produce degrees of infertility. Testicular hypoplasia and degeneration result in abnormal, infertile or sterile semen.

In bulls used in AI service there was significant differences in fertility and this difference was generally not related to observed differences in semen characteristics.¹¹ Fertility differences were largely due to genetic factors carried by the spermatozoa and not due to the environment in the female reproductive tract. The possible incompatibility between the sex cells as in hybrids, and in defective embryos from certain males, as well as incompatibility or possible immunological factors between the spermatozoa and zygote and the dam were dis-

cussed.^{11,17} Immune sera produced against bull semen in cattle caused an antifertility effect, either failure of fertilization or early embryonic death, when used to treat bull semen prior to insemination of heifers. In a recent study no sperm-immobilizing antibodies were found in normal or repeat breeding cows and it was concluded that antibodies against sperm were not responsible for failure of conception in these latter cows.³⁰ In the human, correlations between sperm antibodies and infertility have been inconclusive.

The relatively slow aging of spermatozoa in the male reproductive tract was reviewed and evidence cited to indicate that increased embryonic deaths occurred when these aged sperm cells were used for insemination. In contrast aging of spermatozoa in the female reproductive tract occurs in a matter of hours and it appears that the fertilizing capacity of the sperm cell is lost before changes occur in the genetic material.⁵⁵ Liquid bull semen stored at 5° C. for five days progressively loses its ability to fertilize ova and the incidence of early embryonic death increases.⁷⁶ Fertility based on 180-day nonreturn rates declined from 60 percent for semen used on day 1 after collection to 47 percent on day 5. The results of aging of spermatozoa in frozen semen were similar in that the decline in fertility went from 66 percent with frozen semen used less than 30 days after collection to 55 percent in semen stored over 6 months. This loss of fertility was probably due to chromosome damage, possibly chromosome leakage.

Thus, genetic, congenital and acquired defects of the ova or spermatozoa may result in failure of fertilization or early embryonic deaths and repeat breeding.

Infectious or Traumatic Inflammatory Processes Affecting the Genital Organs—result in repeat breeding due principally to early embryonic deaths. In a few cases where inflammatory processes have resulted in unilateral or bilateral obstruction of the genital tract as described earlier in this Chapter, failure of fertilization may result. Failure of fertilization may also occur in cows with severe salpingitis, metritis, cervicitis or vaginitis characterized by much inflammatory exudate and large numbers of bacteria that would be toxic to the sperm cells resulting in their loss of motility and death. The intriguing new field of the possible role of viruses in the developmental biology and pathology of preimplantation embryos and pregnancy wastage was reviewed.¹⁶ Presently knowledge in this area is very limited.

The infectious bovine venereal diseases of vibriosis due to *C. fetus*, trichomoniasis due to *Tr. fetus* and probably brucellosis due to *Br. abortus*, IBR-IPV virus, "Epivag" virus in Africa, possibly BVD-MD virus and certain pathogenic mycoplasma, ureaplasma or He-

mophilus organisms if introduced into the uterus with semen by artificial insemination can cause infertility and repeat breeding due to early embryonic deaths probably secondary to an endometritis of variable duration. As discussed earlier in this Chapter the above infections, especially the first two, are well-known for their antifertility affects. The virus of "Epivag" produces a severe salpingitis and perisalpingitis in up to 25 percent of affected cattle resulting in sterility due to the obstructive nature of the lesions.¹⁰⁰ Other nonspecific infections of a great variety that can produce an endometritis have also been described and can cause a varying period of infertility. *C. fetus* and *Tr. fetus* are harbored for long periods of time or indefinitely in the sheath and on the penis of older bulls and migrate by their own motility through the cervix into the uterus after natural service. Other nonmotile organisms can seldom pass through the cervical barrier following natural service but can be introduced by artificial insemination. Some of these infections such as *C. pyogenes*, *Ps. aeruginosa*, streptococci, staphylococci, *E. coli*, mycoplasmas, ureaplasmas, *Hemophilus somnus*^{47b,55b} and others may be present in the prepuce and occasionally in infected seminal vesicles of bulls^{47b,55b} and thus be present in large numbers in each ejaculate. Other infections producing endometritis, as mentioned previously in this Chapter, may enter the genital tract at the time of parturition or soon after, in the act of artificial insemination if it is not performed in a clean and sanitary manner, or in miscellaneous conditions such as pneumo-vagina. As has been discussed previously, only metritis or the severe forms of endometritis characterized by exudate in the uterus can be diagnosed clinically. Refined culture techniques and uterine biopsies are needed to accurately diagnose moderate to mild endometritis in the live cow. Pregnancy, however, can occur in the presence of a mild endometritis.^{64,100} Seventeen clinically normal repeat breeder cows had the same infection rate of non-specific bacteria as 46 normal fertile cows 50 days postpartum, or 56 to 58 percent of each group had at least one positive sampling and 28 percent of cultures of both groups were positive. No *C. pyogenes* infection was present in either group. Thus the use of antibiotic treatment for repeat breeders was not indicated.³⁹

It is generally accepted that a young growing zygote seldom can survive in a diseased environment and for optimum fertility a normal or nearly normal endometrium is desirable or necessary. The genital tract, and especially the uterus, has excellent mechanisms of local antibody production, phagocytosis, mucous flow and uterine contractions that can usually overcome an endometritis at the first estrous period or within the span

of 2 to 6 estrous periods. This spontaneous recovery from infection has been well-documented in the postpartum involuting uterus and in vibriosis and trichomoniasis. Therefore by the time the infertile cow with endometritis is classified as a repeat-breeder she is often well on the way toward recovery or has recovered her fertility. This probably accounts for the divergent reports and observations on this subject as reviewed.^{17,23,41,46,69,78,82} Some authors reported only a very low incidence of pathological or inflammatory changes in the genital tracts of repeat breeder cows as cows with clinical infections were eliminated from the classification. Antibiotic and other infusions to correct possible uterine infections in repeat breeding cows may or may not, usually the latter, reveal significant results over nontreated controls. In many repeat breeding cows at slaughter, cultures of the uterus are negative for pathogenic bacteria. Nonspecific bacteria are commonly found in the cervix and caudal genital tract of cows and are always present as contaminants from the prepuce in semen. The presence of antibiotics in the semen used artificially controls or destroys certain infectious organisms such as *C. fetus* but the natural body or uterine defense mechanisms at estrus provide strong protection against infections due to these bacterial or other agents introduced into the genital canal with the semen. This author believes that endometritis due to various infectious agents is a common cause of infertility early in the postpartum period but within a variable time a rapid spontaneous complete recovery occurs. Thus if the repeat breeder cow has a normal genital tract on clinical examination, there is no reason for withholding service. The ability to ascertain this state of the genital tract will vary between veterinarians. Increasing the period of sexual rest to improve conception rates on the next service is uneconomical in the clinically normal cow. Neither a natural or artificial service will prolong the time before conception will occur. Rapid spontaneous recoveries followed by conception are common.

Endocrine dysfunction as a common cause of repeat breeders is probably unlikely since the estrous cycle in these animals has been generally reported as normal except for prolonged postservice periods when early or late embryonic deaths occur.^{17,40} However there is some evidence that a hormonal dysfunction can result in repeat breeding after treatment of cystic ovaries with LH or GnRH or after estrus synchronization with prolonged progestin therapy.

The author previously reviewed the controversial studies on delayed ovulation or anovulation.⁷⁴ The examination of repeat breeding cows 24 to 36 hours and later after service should reveal either delayed ovulation, anovulation, errors in estrus detection or the development

of cystic ovaries noted under stress conditions. The use of the milk assay for progesterone should aid the diagnosis. Delayed ovulation and anovulation are uncommon causes for repeat breeders.^{3,4,17,24,67} If these conditions are suspected the administration of 2000 to 5000 IU HCG or 100 ug GnRH and daily breeding until ovulation occurs might be indicated. The routine use of GnRH and HCG at the time of breeding have not given consistent results nor is there any evidence that the injection of these hormones, shortly after breeding, 3 to 10 days, improves the rate of conception. Therefore their use in these ways cannot at present be recommended.^{25a,89} HCG given 10 days after breeding prolonged diestrus about 5 days.^{25a} Two recent reports indicated that injecting GnRH (100 ug) at the time of insemination in repeat breeder cows improved the conception rate over 15 percent from untreated controls. This treatment did not affect first service conception rates.^{57b,77a} Further study is indicated.

The administration of small doses of estradiol to promote the LH surge early in estrus has not proven practical even with estrus synchronization. As noted under the prevention of conception in Chapter V injections of estrogens at the time of estrus or within several days after ovulation will affect the transport of the fertilized ovum in the oviduct resulting in too rapid transport or "tubal locking" of the ova and death of the zygote. Estrogenic mycotoxins, such as zearalenone, present in feed might cause infertility by inhibition of gonadotropin secretion and ovulation and cause abortion.¹² Injections of oxytocin from day 2 to day 6 after estrus and service causes hypoluteinization of the CL, early embryonic death and shortened estrous cycles. The normal CL at 15 days of gestation contained 270 mg total progesterone while a small hypoluteinized CL with less than 100 mg of progesterone could not maintain the early embryo (See Bovine Reproductive Physiology). A study reported that 57 percent of nursed beef cows conceived on the first service compared to 71 percent of milked cows that conceived.⁹⁷ Services per conception were 1.84 in nursed cows and 1.54 for milked cows.

In a clinical and endocrinological study of 37 first or second inseminations of 10 cows for their third pregnancy starting 80 days after calving comparisons were made between the fertile and infertile services.²⁷ Fertile cows conformed to the generally accepted pattern of regular estrous cycles (17 to 25 days) with termination of the cycle within 3 to 4 days after the C.L. started to regress. The plasma progesterone decreased from near maximum to near minimum (below 0.75 ng/ml) in about 2 days. The onset of estrus and the LH surge occurred in another 24 hours followed by ovulation in 20 to 26 hours. Infertile cows showed evidence of asynchrony

either before or after insemination. Fourteen of 26 cows (54 percent) did not show estrus or an increase in LH within 32 hours after plasma progesterone declined below 0.75 ng/ml. Thirteen of 26 (50 percent) infertile cows that ovulated had low plasma progesterone 6 or more days after ovulation. Nine cases had both defects. Variations in estrogen levels in plasma were large in the infertile cows and might account for failure of the fertilized ova to enter the uterus at the proper time.²⁷ It was believed that the low conception rate of 34 percent was associated with the frequent prolonged clinical ovarian examinations and blood collections. Plasma levels of progesterone during the first 10 days of the estrous cycle may affect fertility. Cows given PMSG in the midluteal phase of the cycle followed by a luteolytic dose of prostaglandin 48 hours later that had plasma progesterone levels of 1.2 nmol/l produced excellent embryos while those cows with levels of 3.9 nmol/l produced unfertilized eggs.^{49b} In another group of heifers receiving embryo transfers on day 7 or 8 postestrus, those having plasma progesterone levels less than 2 ng/ml on the day of transfer had a pregnancy rate of 20 percent compared to a 60 to 80 percent rate in heifers with levels of greater than 2 ng/ml.^{73a} Further similar studies of repeat breeder and normal fertile cows should be conducted.

In a later review of embryonic mortality prior data were summarized by Ayalon³ to show that repeat breeder heifers and cows had heavy fertility losses due to fertilization failure and early embryonic deaths. While normal heifers had fertility losses limited largely to embryonic death and normal fertile cows had low losses in both fertilization failure and embryonic deaths. In repeat breeders the critical period for embryonic deaths is when the morula is developing into the blastocyst at 6 or 7 days especially the latter day.³ This study also examined plasma steroid levels from estrus through day 7 and found progesterone levels for normal cows with normal embryos and repeat breeder cows with degenerating embryos were similar. But plasma estrogen concentration rose sharply on day 6 and 7 in cows with normal embryos but in cows with abnormal embryos it did not rise on day 6 and dropped on day 7. This difference correlated closely with marked rises in ion concentrations of potassium, zinc, phosphorus and especially calcium in the uterine flushings during the days 6 to 8 after insemination. Whether these changes in plasma estrogen and in concentration in uterine flushings were the cause of the embryonic deaths or due to the embryonic abnormalities and deaths will require further study. Protein levels in the uterine flushings were higher in normal cows than in repeat breeders despite the state of the embryo. These studies offer challenging new insights into the

enigma of the repeat breeder heifer or cow.

Although there was little evidence that repeat breeders are due to an imbalance of ovarian secretion,^{17,40} others have noted that progesterone or a progestagen administered 3 to 5 days after service and continued for a variable period of 2 to 3 weeks or longer improves the conception rate in repeat breeder cows over the controls.^{19,22,43,50,73,98} Products used have included progesterone in oil and repositol progesterone at doses of 50 to 100 mg daily. However, other studies have shown such supplementation to be of no value or if given during estrus or shortly thereafter actually was detrimental to conception.⁸⁹ This increased amount of progesterone the first few weeks after fertilization may improve the uterine environment for the zygote so a larger number of embryos survive. In repeat breeders most embryonic deaths occur before the corpus luteum regresses. In fact failure of fertilization or the death of the embryo is necessary for repeated cycles to occur in bred cattle. Starting treatment with progesterone before day 3 or 4 after service may suppress C.L. growth, hasten ova transport or in some other way lower the fertility of normal and repeat breeder cows.

Managerial deficiencies including nutritional deficiencies in the herd are a common cause of lowered fertility and repeat breeding. These must be differentiated from infectious venereal diseases such as vibriosis and trichomoniasis which also are often herd problems. The managerial causes of repeat breeding have become greatly increased with larger herds and the widespread use of artificial insemination. It will probably continue to increase with the trend toward each herd owner or herdsman inseminating his own cows with frozen semen.

It is a significant fact that the larger the herd the greater the infertility or incidence of repeat breeding.^{79b,99,100} Many herdsman can supervise and watch the cows in small herds but in large herds this is more difficult, more time must be spent in observation and more detailed records are necessary. A common cause of repeat breeding is poor or inadequate observation of the cows at frequent intervals each day for signs of estrus. If this is not done regularly, 2 to 4 times a day, up to 20 to 40 percent of the estrous periods may be missed and poor timing of insemination in regard to ovulation results and aging of either the ova or spermatozoa or both may occur (See anestrus). A study of 86 herds of cattle demonstrated that if 1, 2 or 3 cows are presented for service in the same herd at the same time that conception rates were 69.1, 64.5 and 59.2 percent, respectively.²⁹ The lowered fertility occurring when 2 or more cows were presented for service at the same time was due to the tendency to offer cows in suboptimum breeding condition. A summary of

data on fertility in relation to the length of the estrous cycle concluded that there was no practical reason for delaying service because of estrous cycle irregularity if the cow is otherwise normal and the cycle is at least 17 days long.²⁶ Shorter cycles are indicative of cystic ovaries or acute endometritis. The average length of the bovine estrous period is 10 to 28 hours and ovulation occurs 10 to 15 hours after the end of estrus. Cows should be bred within 10 hours before or after the end of estrus for best fertility. This requires frequent daily heat checks and regulated insemination. Bull spermatozoa have a variable life up to 48 hours in the female but highest fertility rates occur within 12 to 24 hours after service. If estrus and ovulation are normal there is very little increase in conception rates, only about 2 percent, in inseminating cows twice, once late in estrus and again 12 to 20 hours later. Calves resulted from insemination from 14 to 34 hours before ovulation.^{1,95} It was demonstrated in 1943 with a large group of cattle, that cows bred at the beginning of estrus had a conception rate of 44 percent, at midheat 82.5 percent, and at the end of heat 75 percent; 6 hours after the end of estrus 62.5 percent; 12 hours, 32 percent; 18 hours, 28 percent; 24 hours, 12 percent; and 36 hours, 8 percent; 48 hours after the end of estrus no ova became fertilized.^{86,87} This indicated that the ovum probably was unable to survive longer than a few hours after ovulation. There is evidence that spermatozoa might have to be in the genital tract about 6 hours before ovulation for optimum fertilization and conception. It seems likely that the excellent fertilization and conception rate reported in one trial may have been due largely to careful and frequent observations for estrus, and to artificial insemination at the proper time of estrus.^{9,10} In a limited study conception rates were similar in 97 cows bred as soon as estrus was detected and in 92 cows bred 12 hours after the onset of estrus.^{77a}

In recent years, in contrast to earlier trials, evidence has shown there can be considerable latitude as to the time of semen deposition in relationship to the time of estrus recognition.^{8,32} Data on 32,400 cows observed in estrus in the AM had a 67.1 to 69.9 percent nonreturn rate if bred that day and a 62.7 percent nonreturn rate if bred before noon the next day. In over 12,300 cows observed in heat in the PM the nonreturn rate for cows bred before noon the next day was 69.9, from noon to 2 PM was 67.4 and after 2 PM the next day the nonreturn rate was 63.8. This data from New York was confirmed in Virginia.⁸ In a beef herd in Colorado 2,091 cows were inseminated with a calving rate of 63.4 percent; 1,019 cows bred after 24 hours after estrus was detected had a calving rate of 60 percent.

However in Texas short estrous periods and low in-

tensity of estrus in Holstein dairy cattle made detection of estrus difficult. About 25 percent of estrous periods would have been missed on twice a day instead of 4 times a day estrous checks.¹⁵ Cows bred immediately after the detection of estrus had a much lower embryonic death loss, especially during the hot seasons of the year than cows bred 12 hours after estrus was detected. Further studies should be made to confirm this latter report.

The effect of nutrition, especially TDN intake and the need for a positive energy balance for high fertility was discussed earlier in this chapter. There is little question but conception rates are better when cows are increasing in body weight. This poses a severe problem for managers of herds with high-producing dairy cows to provide rations and see that cows consume sufficient energy to have a high fertility level. There is no evidence in cattle that increased embryonic deaths occur in overfed animals.³⁶ There is evidence that supplemental iodine, particularly in iodine deficient areas has a beneficial effect on fertility. When supplemental iodine was provided in a controlled experiment in 190 herds with 1572 cows, conception rates on first service in treated and untreated herds were 69.1 percent and 62.2 percent, respectively.⁶⁵ An organic iodine compound was fed orally for 8 to 12 days before the next service in 1036 repeat breeding cows and 58 percent conceived on the first service, while in the control cows conception rate was well below 50 percent.⁵⁸ It is possible that iodine absorbed from the uterus by uterine infusions of an iodine solution exerts a similar effect.

The Production Division of the Milk Marketing Board in England reported that the conception rate in 125 newly established herds was 60.8 percent as compared to 73.7 percent conception rate in 64 other herds in the same area.^{47a} The lowered fertility was probably due to a combination of stress placed on the animals by transport and new surroundings, and the difficulty of the new owners in evaluating the heat characteristics and having the cows inseminated at the proper time. Lowered fertility occurred after the stress of transport and in a new environment.^{47a} Conception rate in 634 cows bred artificially for the first service within 2 months after moving was 54.9 percent; while in over 32,000 first services in cattle born and remaining on a farm the conception rate was 68.6 percent.

Further evidence illustrating the effect of stress on lowered bovine fertility is the reduced fertility associated with high ambient temperatures of over 80° F for long periods in the summer months in the southern portions of the United States. Under hot climatic conditions the duration of estrus was shorter and the intensity of signs of estrus was reduced.³² High temperatures depressed feed

consumption and milk production and resulted in a 10 percent reduction in pregnancy rate.⁵¹ This decline was even greater than 10 percent when frozen semen collected from bulls during the hot summer months was used. Jerseys and Brown Swiss were more resistant than other dairy breeds to the effects of heat. Lowered conception rates to near 20 percent, during the summer months was reported in Arizona and Texas,^{45,80,81} due to low fertilization rates and high embryonic death rates. Monthly pregnancy rates in cows bred from June to October ranged from 17.1 to 36.1 percent, while from October through May they ranged from 44.4 to 61.5 percent. More prolonged postservice cycles are observed in the summer months. An excellent review on embryonic deaths discussed the stress produced by a rise in temperature affecting the spermatozoa before fertilization or the zygote immediately after fertilization resulting in embryonic deaths at a later date.⁸⁸ In reviewing problems of infertility in cattle in a tropical or sub-tropical environment it was noted that Zebu cattle did not increase their metabolism to the same extent when external temperatures rose above 73° F as did the European cattle.⁹² High temperature affected the latter breeds by suppressing estrus and ovulation, causing anestrus and anovulation and causing early death of the embryo.

Thus, during the hot summer months in the southern United States especially in dairy herds, every effort should be followed to keep the animals cool by providing shaded areas or sheds, evaporative cooling or even air conditioning for a portion of the day,⁸⁵ especially at higher elevations, that allow the free movement of air, plenty of fresh water and a nutritious diet with a minimal amount of fiber. This would reduce the severity of heat stress, improve feed intake and increase milk production besides resulting in a reduction in repeat breeding cows (See Anestrus).

In natural service the bull deposits his semen in the proper site, while in artificial insemination there are many possibilities for man to render infertile the bovine sperm cells. These possibilities include: (1) improper extension, freezing and storing of fertile semen. Warming of frozen semen above -79° is highly detrimental to sperm cell viability and fertilizability; (2) improper thawing of frozen semen. This must be done rapidly in a large volume of luke warm or ice water as slow or erratic thawing rates are harmful to sperm cells; (3) insemination should take place promptly, within several minutes after thawing. Thawing semen and keeping it at 5° C. or 40° F for an hour or more is very detrimental to sperm cells; (4) a proper insemination technique should be followed to place the semen in the middle or cranial portion of the cervix, not into the uterus, in a clean and sanitary man-

ner with little or no trauma to the genital tract. Directions provided by the supplier of the frozen semen should be strictly followed if satisfactory results are to be achieved. If liquid extended semen is used, it should be recognized that conception rates decline each day the semen is stored at refrigerator temperatures. In 5744 inseminations in 146 Holstein herds, the conception rate declined from 65.4 percent for first day liquid semen to 45.6 percent for over 3-day-old, stored semen.

For optimum conception rates on first service and a minimal number of repeat breeders, cows should be bred 60 days or later postpartum.¹⁴ The respective conception rates to first service were 39.5 percent for cows bred at less than 40 days postpartum, 51.2 percent for cows bred at 41 to 50 days, 59.4 percent for cows bred at 51 to 60 days, 63.7 percent for cows bred at 61 to 90 days and 65.1 percent for cows bred over 90 days. Similar results were reported by others. In a recent study and review⁹⁶ conception rates at first service postpartum under 30 days were 18 to 37 percent, from 30 to 40 days 45 percent, from 40 to 50 days 53 percent and from 51 to 59 percent for every 10 day interval to 120 days postpartum. In beef cattle a short breeding season was highly desirable. This often required that cows be bred before 60 days postpartum. The percent of cows calving when bred the following number of days postpartum, 11 to 30, 31 to 50, 51 to 70, 71 to 90, 91 to 110 and 111 to 130 was 11.1, 57.7, 77.5, 80.6, 94.14 and 81.8, respectively. The Milk Marketing Board (1968-1969)⁶³ reported the probability of conception was 40 percent if insemination took place between 11 and 31 days postpartum, 55 percent from 32 to 52 days, 62 percent from 53 to 73 days, 65 percent from 74 to 94 days and 68 percent from 95 to 115 days postpartum. If the service interval is shortened by a single breeding cycle, another 6.4 inseminations per 100 cows are required but the calving interval is shortened. These figures were based on hypothetically breeding 100 cows at 84 days postpartum. No harmful effects such as delayed conception, evidence of early embryonic deaths or abortions could be attributed to breeding cows at 35 days or less postpartum except that the cows had lower conception rates.^{70,96} For each 10 days sooner a cow was bred after calving, the calving interval was shortened 8.8 days. Thus, although there was a slight increase in the number of services required for cows bred less than 50 days, there was no increase in lost days and the economic value to the dairyman of calving intervals of 12 months or even less, might be worth the slightly increased number of services per conception.⁷⁰

Palpation of the ovary at the time of insemination should not be done by the lay technician. If an experienced veterinarian or researcher wishes to examine the ovaries to

palpate the Graafian follicle and determine the time of ovulation, it should be done in a gentle, skillful manner to prevent manually rupturing the very thin-walled follicle. The accidental manual rupture of the mature follicle during estrus resulted in conception in 1 of 7, 5 of 12 and 1 of 17 cases, respectively. Less than 20 percent conception resulted from service after this accident.^{1,90,93} Apparently the ova are washed away or possibly caught in the collapsing walls of the unphysiologically "ovulated" follicle.

Although evidence has been presented to indicate that clinically normal repeat breeding cows are similar in some parameters to normal fertile cows, limited embryo recovery, examination and transfer studies have shown significant differences between these two classes of cows.^{25b,56} Twenty-three repeat breeding heifers and 18 normal virgin heifers were bred AI to one highly fertile bull and embryos or blastocysts were recovered non-surgically and examined, the number and percent of normal blastocysts from the virgin and repeat breeding heifers were 23 (74.2%) and 11 (27.5%) respectively. The remaining blastocysts were degenerated or in the process of degeneration. Blastocysts were recovered in 70.4 percent of the collection attempts in virgin heifers and 57 percent of the attempts in the repeat breeding heifers. These differences were highly significant.⁵⁶ In another study it was reported that most infertile beef cows do not respond to superovulation with gonadotropins as efficiently as fertile beef cows.^{25b} Greater numbers of fertilized ova were recovered from the fertile dairy cow donors than the infertile donors, average 6.8 vs. 1.1, respectively. The infertile cows were divided into two groups, those with diagnosed causes of cystic ovaries, endometritis or adhesions which were treated and had two normal estrous cycles before ova collection and those cows with undiagnosed infertility.^{25b} When single ova were collected from unsuperovulated cows the quality of the fertilized ova from the fertile and diagnosed and treated infertile cows and the pregnancy rates (88 percent) following transfer were excellent and similar. But the pregnancy rates following transfer of embryos with similar quality from the undiagnosed infertile cows was only 33 percent and only 21 percent of these cows yielded viable embryos. Thus it would appear that these undiagnosed infertile cows produced viable embryos but had "abnormal" reproductive tracts causing poor zygote transport or a uterine environment unable to support embryos.^{25b}

The convergence of significant older data in several animal species^{32b,51b,57b,c} with a recent study^{39b} based on 984 bovine embryo transfers from superovulated donors compels the author to propose that repeat breeders or problem breeders, especially older females, probably is

due to a combination of factors including: (1) significantly fewer fertilized ova entering the uterus of infertile or repeat breeding females compared to healthy cows (2.6 vs 6.7), (2) significantly increased numbers of infertile bovine females with no ova or embryos entering the uterus compared to healthy cows (21 vs 4 percent), (Since non-fertile ova are retained in the oviducts of problem mares this finding would be more common in the equine species) (3) reduced pregnancy rates in young healthy recipients of visibly normal 6 to 8 day-old embryos from infertile older females compared to normal cows (58 vs 68 percent);^{39b} and (4) aging, "wear and tear" of pregnancy, birth, and uterine disease processes that result in an increase in uterine collagen in pluriparous rabbits,^{57b,c} mares,^{51b} and cows. Reduced blood flow and fewer estrogen and progesterone receptors were present in the older rabbits' uteri,^{32b} and possibly the uteri of older cows and mares, contributing to their infertility. Further studies on this frustrating complicated and multifaceted repeat breeder cow problem is indicated.

Conclusions on repeat breeding—The general and broad physiological and pathological causes of repeat breeding in cattle have been outlined. Many excellent studies on various aspects of the problem have been made and advances have been achieved in the past 25 years. However, the treatment or handling of the problem at present is essentially based on the experience, skill, knowledge and thoroughness of the diagnostic procedures employed by the veterinarian to arrive at the cause(s) and contributing cause(s) for this problem. In some instances it may be necessary to permit a degree of repeat breeding if offspring from a relatively infertile or old sire or dam are desired or if it is desired to shorten the calving interval by early postpartum breeding. If artificial insemination is practiced, a painstaking examination of the frozen or liquid semen and the processes employed in storing semen and inseminating the cow must be undertaken. Just because semen is frozen and labeled, its fertility is not assured! If natural service is used then the bulls and their semen, libido and servicing ability must be carefully evaluated. The diligence and care the owner or herdsman takes in observing and recording heats and services are important. Some owners and managers are not well acquainted with the behavior of cows and have difficulty recognizing estrus.

If repeat breeding is a herd problem, the semen or bull used, the presence of infectious venereal diseases or the improper observation, recording, breeding and management of cows or all three areas may be at fault. If individual repeat breeding cows are the problem, then a wide variety of causes may be considered. With the many causes for repeat breeding, it is highly possible that in

a poorly-managed herd repeat services in a cow could be due to a different cause or combination of causes at each infertile estrous period.

Occasionally genetic, congenital or acquired defects or obstructions may be present preventing the union of the spermatozoa and the ovum. Genetic or acquired damage may affect the ova or spermatozoa. In treating repeat breeding cows with normal genital tracts servicing the animals each heat period at the proper time with spermatozoa from a highly fertile bull is imperative. The few cows that have a history of repeat breeding each year for several years or more should be culled.

Endocrine malfunction in repeat breeder cows is apparently not common except in occasional cases of an-ovulation or delayed ovulation which requires further study by a number of investigators under a variety of stress conditions and in many herds. Administering progesterone therapy for a variable period starting 3 to 4 days after service and continuing for 8 or 10 days shows promise in the treatment of certain cows, but further study and trials are indicated. Administering progesterone, estrogens or other steroid hormones before or at service is not indicated.

Endocrine therapy in most repeat breeders is unsuccessful, especially if used empirically and without an understanding of reproductive endocrine physiology. In sporadic infections of the uterus causing repeat breeding, spontaneous recovery in a variable, usually short few weeks or months, is the rule. Infusions (20 to 50 ml) of weak (2 ml of Lugols/100 ml of saline) iodine solutions seem to be as good or better than any other intrauterine therapy given 12 to 36 hours post service. Antibiotic infusions given within 10 to 15 minutes after insemination may have a detrimental effect on conception.²⁰ In certain herd or individual cow problems uterine biopsy and culture might be helpful in making a diagnosis.

When one considers the multiplicity of the direct and indirect or predisposing causes for failure of fertilization or early embryonic deaths, the magnitude of the diagnostic problem posed by this problem is challenging. Particularly so in problem herds where careful study will usually indicate the cause and in individual problem cows where the exact cause may be impossible to determine with accuracy. Treatment of these latter cases should never become routine or empirical, but these cases should be studied more carefully and in greater detail and the recommended therapy should be given based on knowledge concerning reproductive physiology, use of highly fertile males, servicing at the proper time of estrum, repeated matings, patience and, if necessary, conservative therapy that will not interfere with or prevent fertilization and early embryonic development. Every decade has

brought forth new knowledge and insights on this complicated, multifaceted problem. Further studies on the causes and possible rational therapy of repeat breeding cows are needed.

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The Postpartum Period

In attempting to achieve a desirable, economically necessary 12- to 13-month calving interval, the interval from calving to conception must be 85 to 115 days, respectively, since the duration of gestation is fixed at 280 days. To achieve this goal, breeding of cows that have normal calving and postpartum periods should begin at

50 days after two postpartum estrus cycles, 14 to 18 days and 30 to 38 days. These are necessary to result in good conception rates. This then allows two breeding periods between 50 and 85 days or three breeding periods between 50 and 115 days. Services per conception should be about 1.7 per conception or less which would result in 87 percent of the cows pregnant by 110 days (50% conceptions on 1st service, 50% conceptions on 2nd service or 76% of the cows and 50% conceptions on third service or 89.0% of the cows).¹⁶ Breeding prior to 50 days postpartum is generally not desirable because of reduced conception rates (more services per conception)¹⁸ and this practice could cause an abbreviated dry period. Forty-two days has been shown to be a maximum necessary for high milk production.³ For a herd to average a 12-month calving interval the largest number of breedings resulting in conception should cluster around 50 to 110 days postpartum. Economic losses occur when large numbers of conceptions occur earlier than 50 days or more than 100 days. In 56,000 cows in 376 herds it was shown that maximum, total milk production was achieved at a calving interval of 385 days or 375-395 days. Cows bred early in the postpartum period with a calving interval of 343 days averaged 15,700 pounds of milk vs 16,300 pounds produced by cows with a 385 day intervals, a difference of 600 pounds or about 1.6 pound per day.^{12b} Correction of factors causing prolonged calving intervals is more important than early postpartum breeding to an economically profitable production record for a herd. The frequency distribution of observed postpartum estrous periods, services, and calving intervals should be tabulated for study.

Therefore the early onset of the observation of and recording of regular postpartum estrous cycles of all cows is imperative. Cows with milk fever, retained placenta, metritis, postparturient diseases of ketosis, displaced abomasum, acute mastitis, failure to return to a level or positive energy balance, cows developing cystic ovaries and owners failing to detect cows in estrus, all result in a delayed return to service and a prolonged calving to conception interval.^{1,7,11,19,21} The incidence of reproductive disorders in the postpartum period was studied in 4093 lactations in 22 dairy herds in N.Y. State:^{15b}

	Incidence (Percent)	Aver. days to 1st service	Conception Rate 1st service	Breedings per Conception	Days open
Lactations with no reproductive disorders	78	81	51	2.1	103
Lactations with metritis*	15	89	36	3.1	110

	Incidence (Percent)	Aver. days to 1st service	Conception Rate 1st service	Breedings per Conception	Days open
Lactations with retained placenta, without metritis	4	88	42	1.6	106
Lactations with ovarian cysts treated more than once or after 60 days postpartum**	1.5	103	25	4.6	149

*Metritis occurred in 24% or 49% of dystocia and retained placentas, respectively.

**Ovarian cysts diagnosed prior to 60 days postpartum (2% incidence) did not impair performance.

In a study of 106 postpartum cow's genital tracts *C. pyogenes*, coliforms and streptococci were isolated most frequently. Abnormal uterine involution with a purulent discharge was most commonly associated with *C. pyogenes* infection and resulted in an increased number of services for conception and in cows culled for infertility.^{16b} Cows with a clear vaginal mucus at estrus do not require therapy while the presence of a purulent vaginal discharge should be treated even if the cervix and uterus are involuting normally. Young 2 to 3 year-old cows had a higher first service conception rate than did older cows, 61 vs 35 percent respectively. In this study, one or more postpartum diseases also reduced the first service conception rate and the latter was negatively correlated with milk production.^{16b}

Calvings should be in a clean, well-bedded with straw or hay, disinfected stall or a clean pasture to avoid postpartum retained placentas and postpartum infections (See Chapter XI). In older cows prompt treatment of incipient milk fever or retained placenta with calcium products and oxytocin and possibly parenteral antibiotics is imperative. Dry cow therapy and dipping of teats should be practiced when drying the cow off and teats should be dipped for a week or so before calving. Postpartum examination of the cow at about 21 and/or 35 to 45 days¹⁷ is indicated to be certain normal involution and estrous cycling is occurring and that postpartum infections or cystic ovaries have not developed. If cystic ovaries have developed prompt administration of GnRH or HCG is indicated. In older cows or high-producers it may be desirable to give 100 to 250 ug of GnRH on the 12th to 14th postpartum day, or when follicles 1 cm. in diameter are present, to promote ovulation, normal corpus luteum formation and estrous cycling and prevent the development of luteal or follicular cysts.²² Evidence reported to the author indicated that manual massage or examination of the bovine uterus per rectum 8 to 15 days postpartum might stimulate uterine activity, the estrous cycle and hasten uterine involution and result in a greatly reduced

calving to conception interval.^{1a,b} Uterine examinations 20 to 35 days postpartum did not result in such pronounced effects.^{1b} Further controlled studies are indicated.

A nutritional program should be established for the dry cow to avoid overconditioning and the problems associated with the "fat cow syndrome" at calving, and then as milk production increases after calving, energy intake should keep pace so the cow is not losing weight the first 90 days postpartum.^{1c,10} A negative energy balance is associated with postpartum anestrus. If this is prevented earlier estrous cycling occurs which improves the conception rate after 60 days postpartum. Careful, frequent observation of all postpartum cows during the early and late daytime hours and one-night time period is necessary^{7,19} to detect, record and breed or inseminate the cow with highly fertile semen at the proper time between the middle to just after the end of estrus. Insemination should be performed by a skilled technician. Heat detection aids such as Kamar heat detectors or chalk or paint on the rump may assist in estrus detection. Careful observation of all bred cows, especially 20 to 23 days after service and pregnancy examinations at 40 to 45 days are imperative to prevent many missed heat periods.^{19,23} All cows not previously diagnosed as definitely pregnant should be examined at each herd visit at preferably monthly or semimonthly intervals by a knowledgeable veterinarian.

For certain cows that are cycling as noted by the presence of a normal mature corpus luteum but estrus have not been observed, an injection of a luteolytic dose of prostaglandin (**Lutalyse** 20 to 35 mg or **Estrumate** 250 to 500 ug) injected IM once or twice at 10 to 12 day intervals should be followed by breeding at the next estrus in 2 to 5 days or at 72 and 90 hours after the injection of prostaglandin.¹⁴ (See Estrus Synchronization discussed in this Chapter.) If postpartum metritis or endometritis develop prompt intrauterine therapy with adequate antibiotics or antiseptics is indicated together with

prostaglandins to establish a normal estrous cycle. If natural breeding is practiced, cows should be vaccinated against vibriosis one month before breeding.

Beef cows suckling calves especially twin calves usually have a much longer interval from calving to first estrus than dairy cows not suckling calves. This is a serious problem in beef herds, particularly beef cows of Brahman or crossbred Brahman breeding.^{13,20} It is a lesser problem in the Angus breed. This "lactational or nursing anestrus" prevents many beef herds achieving a 12 or 13 month calving interval. A review of a number of studies on suckled European beef cows showed that variable periods of anestrus from 27 to 150 days followed calving.⁹ In Brahman or crossbred Brahman cows this period of anestrus may extend from 100 to 200 or more days postpartum. Apparently there is also a genetic component to the length of the postpartum anestrus. Other factors compounding this prolonged postpartum anestrus in beef herds is the level of nutrition and condition of the dam before and after calving and the age of the dam. Thin heifers nursing calves frequently have very prolonged postpartum anestrus periods.^{20,21} Increased dietary energy intake pre- and postpartum in suckled postpartum beef heifers increases LH secretion and shortens the anovulatory periods.^{2a}

Although much further study is required on the critical postpartum period, it has been shown that plasma levels of the prostaglandin metabolite were high for 7 to 23 days postpartum in cows with a normal parturition and uterine involution. If a uterine discharge with delayed uterine involution developed elevated prostaglandin secretion was present for a longer period of time.⁸ Progesterone levels remained low until prostaglandin release from the uterus had ceased which in normal cows was about 15 days postpartum. During this early postpartum period circulating LH levels were low and secretory spikes or episodic releases of LH were suppressed by suckling.⁹ Weaning resulted in an increased number of secretory spikes of LH followed by estrus. The suckling intensity of single or twin calves is correlated closely with the length of the postpartum anestrus. Since suckling releases corticosteroids in nursing cows these hormones may suppress the release of pituitary LH by GnRH. When calves were weaned at 3 days postpartum, estrus and ovulation occurred at 17 days. If calves were allowed to suckle only once a day starting at 30 days postpartum, the postpartum interval to first estrus was 69 days vs 168 days in Brahman crossbred heifers allowed to suckle their calves normally.¹³ After weaning of their calves 25 to 42 days postpartum, most anestrus beef cows show estrus within 10 days. However about 80 percent of these cows return to estrus, a short cycle, in 7 to 12 days.

Insemination at the first estrus is usually infertile even though ovulation and fertilization occurs. But insemination at the second estrus followed by a normal length cycle resulted in a normal conception rate. The cause of the failure of pregnancy on the first breeding after weaning is apparently due to early regression of the corpus luteum, about the seventh day that also causes this common short first estrous cycle.^{12a,13a,b} The cause of this early CL regression after the first ovulation and estrus after weaning requires further study.

In another study, suckled beef cows developed small follicles by 16 to 18 days postpartum but estrus and ovulation did not occur. However, if 250 mg GnRH was given on days 27 to 29 about 50 percent of the cows ovulated. If calves were weaned for 24 hours before given GnRH the response improved. Apparently suckling suppressed the release of LH necessary for follicle maturation and estradiol secretion.^{4,6} However, weaning is not a practical solution for postcalving anestrus in most beef herds. Modified weaning programs of once daily suckling starting at 30¹³ or 50 days postpartum or weaning for 48 to 60 hours (Shang treatment) combined with a short progestogen treatment,¹⁵ have resulted in some success in establishing earlier estrous cycles when combined with other synchronization programs such as progesterone, and GnRH^{2,15} (See the Postpartum Period and Estrus Synchronization in this Chapter). Further studies on the hormonal, nutritional and managerial aspects needed to shorten the postpartum anestrus period in beef cows suckling calves are needed.

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Herd Reproductive Health Programs

Foote reviewed the inheritance of fertility and concluded:

"The fertility problem of greatest economic importance in a herd or population is over-all breeding efficiency. As this has been measured by services per conception, percent nonreturns, first service to conception, calving interval, etc., additive genetic variance has been very small and heritability has been approximately zero. Thus, selection for these traits would not be effective and would be at the expense of other traits of economic importance which show a greater response to selection. **Infertility in cows appears to be primarily a management problem.**"⁷

Reproductive health programs for both dairy and beef herds are practical and essential for successful herd management. The veterinarian plays a highly important role as a consultant and advisor to the herd manager or owner in setting up the reproductive health program and maintaining its effectiveness to achieve the goal of a calf per cow every 12 to 13 months. In dairy herds fertility can be measured by a number of criteria and realistic herd goals are: a pregnancy rate of 60 percent on first service, an average of 1.5 to 1.7 services per conception, a calving interval of 12 to 13 months per cow or a maximum of an average of 100 days from calving to conception. A calving interval of 12 months produces the highest milk yield and the greatest number of calves. The most common causes of a longer calving interval are long intervals between parturition and first service, long intervals after service if conception has not occurred, or too many services, 5 or more, before conception. Thus the calving interval is more important than services per conception in measuring herd fertility.⁵ Records should be set up so that periodically they may be reviewed to see

if the herd is reaching, maintaining, or failing to reach these criteria necessary for a successful reproductive health program. Small, practical reasonably priced computers are or will shortly be available for farmers and veterinarians. In the dairy areas Dairy Herd Improvement Associations (DHIA) offer computer services on many aspects of dairy herd and farm management. With larger herds of cattle becoming more common the computer is or will become an essential tool for the manager and veterinarian. The computer is primarily an information storage, retrieval and analysis system and all 3 functions should be utilized.²¹ Records should be maintained in such a fashion that the cause or causes for infertility such as anestrus, silent estrus, repeat breeders, cystic ovaries, semen from certain bulls and etc. can be readily ascertained. In beef herds an achievable goal is a 90 percent calf crop within a 3-month breeding period. To reach and maintain these goals requires the close cooperation of the herdsman, manager, owner, inseminator, and veterinarian.

In dairy herds a herd reproductive health program requires a visit by the veterinarian to examine the cows every one to two months or in larger herds more frequently. Less frequent visits are unsatisfactory. Charges for such regular visits have been made by various veterinarians based on the visit, on an hourly rate, or on a flat rate per cow per visit or year. The former two methods of charging are generally preferred because then the manager or owner of the herd prepares for the visit by getting his records in order, has his cows in and his help organized so the visit goes smoothly and rapidly. Since reproductive health is the core of a general herd health program, the reproductive health program is usually established first and then other aspects of herd health are added to it as the farmer and veterinarian desire. Education of and cooperation with the farmer and concern for the herd by the veterinarian are essential.

Records must be maintained in a herd reproductive health program. Each cow must be properly and permanently identified. In large herds this identification should be readily ascertained by observation, often from a distance, to facilitate recording and isolation or restraint for breeding or examination. Reproductive herd health forms should be fairly simple and practical for the average dairy farmer to maintain on a daily, monthly and yearly basis. The type of record used should be tailored to the preference of the veterinarian and farmer. Different record forms have been described and used by many veterinarians.^{3,6,12,14,15,16,19,24} Records must identify the cow, indicate the time of calving or abortion, heats, services and pregnancy examinations. They should also include all genital examinations noting normal and abnormal

findings and the therapy administered.

These records might also be expanded to include the sire and dam, the number and sex of offspring, abnormalities at calving, vaccinations and time administered, the bull used for service of the cow and whether AI or natural service was employed, and the results of blood or other diagnostic tests. These records may further be expanded to include other health records and examinations such as mastitis and other disease problems and even production records. Records of the date of purchase of cows and the name of the previous owner are often desirable.

Any herd reproductive record system should include provisions for daily referral to the records or placing entries in them. In larger herds a herdsman's **daily report form** is helpful to record calvings, breedings, vaccinations and other abnormalities and treatments. **Estrus expectancy charts** are available from feed companies, AI organizations, and extension services and are very helpful to dairymen to note heat dates and service dates so they are reminded when to watch certain cows. More permanent records may be made on forms kept in loose-leaf notebooks, Kardex files, and card files specifically designed for reproductive health programs. These may be made up by the veterinarian or stock forms obtained from one of the above sources. These records should be available in the barn or near it in a clean, dry location free of dust, dirt and excessive moisture.

Several interesting recent innovations to herd reproductive health records have been made. One is the method followed in North Carolina to computerize these records so each month a farmer receives this reproductive record on his cows along with the DHIA record so he knows the calving intervals, breeding dates, and when to have the cows checked for pregnancy. This greatly aids him in maintaining the goals of good reproductive health and requires a minimum of record keeping by the farmer.^{10,11,16} Other states have adopted this program. A practical breeding control "wheel" now being produced by Agway Inc. of Syracuse, N.Y. was invented³ that is an ingenious device that is kept in the dairy barn and records the current reproductive status of every cow which can be determined at a glance. It has proven to be an incentive to herdsman, by its simplicity, to maintain reproductive health records, watch cows for estrus and breed them at the correct time. Other methods for keeping reproductive records including peg boards, black boards and etc. have been reported. Most good record systems require the veterinarian to assist the farmer in developing and organizing a practical system both can follow and use. Then it requires constant encouragement on the part of the veterinarian to have the farmer maintain the rec-

ords in a careful, routine, up-to-date manner.

Management practices—In most cattle herds the major cause of infertility and repeat breeding is improper or negligent management practices. Most infertility problems, such as improper heat detection, are herd problems and require a preventive medicine program in which the veterinarian must become an active part of the farm management to be effective.

Young breeding stock should be properly reared by providing nutritious and balanced rations and proper disease and parasite control including vaccinations so that early and planned breeding of virgin heifers can occur at the desired time.

The breeding herd should be fed sufficient balanced rations so that regular estrous cycles occur and the females are in an optimum breeding condition and on a positive energy balance at the time of service. Nutrition should be such that cows at the end of gestation are not too fat nor too thin as both of these conditions predispose to calving and postpartum disease problems that affect the fertility of the herd.

Sanitation and hygienic practices at the time of calving should be followed to prevent postpartum uterine infections and delayed conception. **Diseases affecting the reproductive system** such as brucellosis, vibriosis, trichomoniasis, IBR-BVD, leptospirosis and others may be controlled by eradication and quarantine methods so as to maintain, as nearly as possible, a disease-free closed herd. Since this is usually not possible in large commercial herds a proper and regular vaccination program should be instituted. All purchased stock should be isolated from the herd for 30 to 150 days and tested for possible infectious diseases. It is preferable to purchase young animals under 6 months of age as replacement stock to avoid the common venereal diseases. Decisions in regard to the various methods of disease control must be made on the basis of the herd history and management practices, the possible dangers from exposure to disease by neighboring cattle, and the nature of the diseases common in the area. Inbreeding should be avoided and close line-breeding should be carefully monitored so that hereditary defects can be culled from the herd and good fertility can be maintained.

The **detection of estrum** is of great importance especially in a herd being bred by artificial insemination. There is no substitute for frequent careful observation of the nonpregnant cows, recording of the estrus and prompt notification of the inseminator so that future estrous periods may be detected or so that a high conception rate on first or subsequent services can be achieved. Cows should be watched closely for estrum. The herd should be turned out or watched closely for thirty minutes or

more a minimum of two and preferably three or four times a day. (See Anestrus.) Cows should be checked for estrus at times other than milking or feeding and particularly at least once during the late evening or early morning hours. This is necessary in tropical climates where estrous periods are shorter and the intensity of estrus is reduced. This practice is necessary during the winter months when dairy animals may be closely confined in stanchions. Utilizing some form of heat expectancy chart or the regular veterinary examination of the genital tract of open cows to predict the time of estrus are very helpful in breeding cows at the proper time in the postestrous period when a bull is not turned with the herd. Normal cows should be bred at the proper time of each estrous period with highly fertile semen to achieve the best and earliest conception rates.

Highly fertile active bulls with a strong sex drive and free of infectious venereal diseases should be used as sires. If artificial insemination is employed the fertility record of the bull should be noted to be certain of the high fertility of his semen. The semen should be stored, handled, thawed and inseminated in a manner to maintain and promote the high fertility of the spermatozoa. If cows in the herd are handbred naturally to a number of breeding bulls, the records of all cows bred by each bull and the date should be recorded so that if infertility occurs in the cows the bulls' fertility records can be examined for evidence of decreased fertility in a certain or several bulls. Switching cows back and forth between bulls at different natural services is a poor practice as venereal diseases are readily spread in this manner. If a cow fails to conceive to natural service to a certain bull, she should be bred by artificial insemination to other bulls on subsequent services.

All cows in the herd, not already safely pregnant should be examined at each regular monthly, or more frequent, visit of the veterinarian to 1) determine pregnancy if breeding has taken place 35 or more days ago, 2) to determine if normal uterine involution is occurring by an examination between 15 and 40 days postpartum, 3) to determine if any pathological condition such as metritis, adhesions of the oviduct, cystic ovaries and other lesions or diseases, including anestrus, may be present that require treatment, and 4) to determine the physiological state of the normal nonpregnant genital tract and the approximate time to expect estrus and whether service at the next estrus is desirable. If the decision of which dairy cows to examine is left to the farmer or herdsman some infertile, diseased, or nonpregnant cows might be omitted from the examination. It is very helpful for the farmer to prepare a list of all the nonpregnant cows and their breeding history prior to the visit by the

veterinarian. This requires the farmer to keep his records up-to-date and to have all the cows to be examined confined. It also saves much time for the veterinarian as he examines each cow. This type of complete examination of all nonpregnant cows gives an accurate herd picture of the nature of the fertility or infertility in the herd at the initial visit or at regular intervals throughout the year.

Miscellaneous herd management factors The herdsman, owner or manager who is in daily close continuous contact with the herd is the most important person determining the success of a reproductive health program. He should be a person who is properly educated and motivated or the program is bound to fail.

Beef herds, besides some of the aforementioned practices, may require different measures for controlling reproductive diseases than do dairy herds.^{4,23} In beef herds each cow must calve each year to be profitable. The breeding season is shorter than in dairy herds, 45 to 90 days, and conception early in the breeding season is highly desirable requiring proper nutrition of the herd. The best means of expressing reproductive efficiency in the commercial range beef herd is the total pounds of calf weaned divided by the number of cows and heifers exposed to breeding in a calendar year. Calf crop equals the percent of cows bred times the percent of conception times the percent of conceptions weaned. If only 50 percent of the cows are bred and only 50 percent conception results then the calf crop is 25 percent or less. Early prompt conception of heifers and cows is essential because of the short breeding period necessary to produce heavy, large calves. To produce early puberty and to obtain early estrus after calving, heifers should gain 1 lb per day from weaning through breeding and weigh at least 650 lbs at the start of the breeding season, and cows should be in good condition at calving and should gain 0.5 to 0.75 lbs per day until the end of the breeding season. Thus adequate rations and sufficient energy are essential for the onset of the estrous cycle and good conception rates.²³ Provision for adequate numbers of fertile, active bulls is essential. If young bulls are used more "bull power" is necessary. Cows that fail to conceive should be detected by a pregnancy examination of the herd in the Fall and probably culled. In range cattle where it is nearly impossible to maintain a "closed" herd, vaccination, especially against vibriosis, brucellosis, leptospirosis, IBR and BVD and possibly other diseases, is highly desirable. If the beef herd is to use artificial insemination, the riders, preferably two or more, should bunch the cows at the feed bunks twice a day, usually morning and evening; the cows should be divided and put into small pastures and pregnant cattle should be kept separate from nonpregnant cattle for easier observation of estrus. Often

sorting the fat range cows and thin range cows into separate herds and feeding according is economically advantageous.

Newly assembled herds often exhibit an infertility problem because of a variety of diseases that may be present. It is best to breed these herds by artificial insemination with highly fertile, disease-free semen. If females are brought into a closed herd, they should be bred by artificial insemination for several years. Every effort should be made to avoid the introduction of a venereal infection carried by a bull into the herd. All aborting animals should be carefully and promptly isolated and the fetus and placenta should be examined by a veterinarian and a good laboratory and blood samples taken to detect the possible cause of the abortion. The aborting animal should be treated and maintained in isolation until genital discharges cease. In tropical or subtropical areas measures should be taken to reduce the stress of high ambient temperatures and its effect on fertility in both the heat-tolerant bull and cow.^{9,18} Other diseases especially parasitic diseases should be controlled. Lame cattle lose weight, fail to show signs of estrus and have lowered fertility. Impotency in bulls is frequently due to overgrown, diseased feet that need trimming, and arthritic lesions. There is little evidence that stress or fright in cattle due to restraint at the time of service has any significant effect on the conception rate. Emphasis should be placed on diagnosis and prevention rather than treatment in herd reproductive health programs. Four major areas for improved efficiency and economic returns for a dairy or beef herd in which a trained veterinarian can have a major role are: control or prevention of disease-related losses, maintenance of good reproductive performance, and to provide advice, and possibly analysis, to achieve the maximum conversion of feed to milk or beef at the lowest cost, and prevent continuing problems associated with rapid genetic improvement.²⁵

Since the veterinarian that specializes in herd health or herd reproductive health programs is occasionally not the "regular" veterinarian that handles sporadic emergency problems and regulatory tests in the herd, it is highly important that he conducts his practice in an ethical manner, consults with the local veterinarian and AI technician, as well as the herd manager or owner and thinks and speaks well of his colleagues. He should practice the "Golden Rule." Often times it is necessary for the local practitioner to carry out recommended treatments and therefore it is important that he understand the reasoning behind the therapy.

The literature on uterine involution after calving and the earlier work on the optimum time to breed cows following calving was reviewed.¹⁷ (See also the Post-Par-

tum Cow.) Although optimum conception rates on first service occur from 60 to 120 days after calving, breeding cows from 40 to 60 days after calving if no abnormality was present, resulted in about a 50 percent conception rate with no subsequent adverse effects on the pregnancy period. Thus if diseases of the postpartum uterus could be avoided or reduced and earlier breeding, down to 50 days postpartum, was practiced, it would be a highly valuable method of reducing the calving interval with only a very slight increase in the number of services per conception.

Ideally only normal, healthy, highly fertile females and males should be mated. It is recognized, however, that both bulls and cows may vary greatly in their level of fertility. As the fertility of the female declines the fertility of the male she is bred to is of greater importance if a good conception rate is to occur. This was illustrated and discussed in humans.²⁰ The fertility index of a couple resulted in prompt conception when both partners were relatively quite fertile. Delayed conception occurred when either the male or female was subfertile or below the borderline index of fertility, and conception was unlikely when both male and female partners were subfertile or below the borderline fertility index. Therefore since highly fertile bulls, especially in AI service, are well known, cows of lowered fertility should be bred to them.

Bartlett has proposed an interesting and significant model to explain the importance of the major factors that enter into the determination of the fertility level of any herd.² These major factors concerning herd fertility are: 1) the fertility of the cows at the time of service, 2) the fertility of the bull or semen, if AI is used, and 3) the efficiency of the management including heat detection, nutrition, timing of insemination, efficiency of the technician, veterinary consultant and etc. If theoretical percentages of 90, 90 and 90 were applied to these three factors on a series of first inseminations the percent of calves born would be 73 percent, or $90 \times 90 \times 90$ since these factors are not additive. If the fertility of the bull was only 50 percent then $90 \times 50 \times 90$ would equal 40.5 percent calves born. The pregnancy rate can be no higher than the lowest value of any of the 3 factors. This illustrates the importance of careful veterinary supervision of the reproductive health of the herd to insure that all factors are maximal. The great economic importance of a herd reproductive health program has been illustrated.^{8,14,15}

In concluding this chapter on infertility in cows the following quotation from Bartlett is concise and applicable: "For some infectious diseases, relatively effective prophylactic and combative procedures have been developed; dairymen and veterinarians need only to take

cognizance of the established precepts. However, our present inability to cope rationally with certain other conditions and the meagerness of the knowledge of their total effects and causes must be recognized. Well-directed, well-supported scientific research is the only source from which the necessary facts can be obtained. Such research merits the encouragement, interest and support of the cattle industry and veterinary profession alike. It is obvious that the causes of lowered reproductive efficiency are exceedingly numerous and the problems of achieving optimum reproductive efficiency exceedingly complex and broad in their ramifications. No panaceas must be expected. Precise diagnoses whenever possible, rational corrective actions when indicated, and trained, intellectually honest advisors mark the sound course. There should be no place for the triflers, five-day specialists, self-confident, self-styled, handyman experts and quack remedy peddlers parasitizing and exploiting the field today."

"For the cattelman, consistent observance of sound management and animal hygiene practices is imperative. The keeping of precise, permanent records, together with a system of regular, physical examinations for pregnancy, will reveal any general occurrence of reproductive failures at the onset and by permitting early treatment or disposal of affected animals, will keep to a minimum the economic reverses resulting from infertility."^{1,2}

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Chapter XIV

INFERTILITY IN THE MARE

With the near demise of the draft horse industry early in the twentieth century in the United States and other countries very little research and study was undertaken in theriogenology in the horse compared to that in food-producing animals. In the last 20 years with the advent of increased interest and development in, and income from, the recreational and racing aspects of the horse industry, much equine research and increased knowledge has been developed. This renewed basic and applied research in equine physiology, pathology, endocrinology and infectious diseases undertaken in many countries has resulted in the recent outstanding publications and reviews by Ginther (115), Rossdale and Ricketts (239) and Proceedings of the First and Second International Symposia on Equine Reproduction (Supplements 23, 27 and 32 of the *Journal of Reproduction and Fertility*) edited by Rowlands, Allen and Rossdale.

Fertility in mares is generally considered to be lower than that of the food-producing domestic animals. This impression or fact has been largely caused by the photoperiodicity of mares resulting in a normal breeding season extending from March to September in northern latitudes and by further restrictions imposed by man on the breeding season of mares in the equine racing industry. The Thoroughbred and Standard bred breed organizations by their acceptance of the artificial requirement of the January first birth date for racing horses imposed by the English Jockey Club in 1833, changing the physiologic original date of Mayday established in 1751, has contributed importantly to the fertility problems in these and other sporting or recreational breeds of horses.²¹²

Caslick⁷⁵ stated that the three chief reasons for infertility in mares were (1) the shortness of the breeding season, (2) failure of the mare to have a normal estrous cycle, and (3) genital infections. The latter condition can be largely controlled by preventive practices, hygiene and treatment so is the least important of the three causes for infertility in the mare even though certain "infection-prone" older mares may not be eliminated as promptly as they should be from the broodmare band. The former two causes of infertility, the shortness of the breeding season and irregularities of the estrous cycle of the mare,

are closely related. Usually less than 30 percent of barren or maiden mares, unless they have been stimulated artificially by a lighting regimen, are cycling and ovulating at the beginning of the breeding season, January through March in the racing breeds in northern latitudes.^{157,211} Furthermore, the requirements of a short breeding season in these breeds abruptly terminates the season in July just as nearly 100 percent of these mares are exhibiting normal reproductive cycles and ovulations.

Other factors that may play a role in the reduced fertility of racing and recreational mares and stallions, different from the food-producing animals, is that they are selected largely for their racing ability, pedigree or owner's whim rather than for their fertility. One can speculate that prior to the description and wide-spread adoption of the Caslick vulva-suturing operation in 1937,⁷⁴ these mares, especially in the Thoroughbred breed, with poor peri-vulval conformation would have remained barren and not passed their genital configuration on to their female foals¹⁸² and the frequency with which this operation is now performed would not have risen to its present level.

In 1940 Day⁸⁸ estimated the average fertility of draft mares usually bred to a stallion that was transported around the country was 60 percent, the fertility of Thoroughbred mares managed under better conditions was 66 percent and the fertility of ponies running the year around on pasture with a stallion was over 90 percent. These estimates, even with our improved knowledge, remain similar to conception and foaling rates from 1950 to 1972 in the Australian Stud Book averaging 66 to 73 percent and 60 to 64 percent, respectively.²¹² In 1968 fourteen breeding farms in the US comprising 6 breeds reported nearly 100 percent fertility in one pony stud; but only 75 percent and 66 percent conception and foaling rates respectively in 5 intensively managed Thoroughbred farms. Farms with Appaloosa, Arabian and Quarter-horses had from 73 to 93 percent conception rates and 65 to 93 percent foaling rates with the highest rates being achieved on farms that practiced some pasture breeding.¹⁴⁵ Ginther⁴⁵ summarized data on published equine pregnancy rates which ranged from 75 to 84 percent per

breeding season. In another report from England on 852 Thoroughbred mares on 82 farms or studs, 229 or 27 percent of the mares were not covered in 1971. Of the remaining 623 mares that were bred, 77.9 percent conceived and 69.7 percent produced a live foal that survived 6 weeks.¹⁶⁶ But of the 852 total mares in the survey only 50.9 percent produced a viable six-week-old foal. In another survey 838 Quarterhorse mares on 5 farms and 939 Thoroughbred mares on 7 farms the pregnancy rate for service(s) in the first estrus the mare was bred was 51 and 43 percent, respectively, and the cumulative pregnancy rate after 5 service periods was 84 and 75 percent, respectively.²⁶⁸ The first-service-period pregnancy rates for maiden, barren and foaling mares were 44, 40 and 54 percent, respectively. The pregnancy rate for foal heat breeding vs non-foal-heat breeding for Quarterhorse and Thoroughbred mares was 58 vs 65 percent and 41 vs 67 percent, respectively. A significant difference was noted between the fertility of the two breeds of horses and foal-heat and non-foal-heat conception rates in Thoroughbred mares.^{18,268}

All mares should be fed an adequate ration of green roughage with some legume, preferably clover. Legumes contain a higher supply of minerals than does timothy. Good pasture supplies roughage in the best form as well as exercise. Grain intake should be adequate to maintain condition and supply the energy and protein needs of the mare. Fresh water and iodized salt should be available at all times. Most breeding mares are fed and cared for in an adequate manner but if they are not, the same deficiencies and symptoms affect them as affect cattle. If the feed is adequate, trace minerals and vitamin supplements are seldom necessary.^{248,265}

Because of the shortness of the breeding period it is essential that all mares to be bred are normal and healthy at the beginning of the season. This requires that barren mares be examined in the fall months and treated if necessary. All apparently pregnant mares should be examined at this time to make certain that an early abortion at 25 to 90 days did not occur. Pregnant mares are usually vaccinated to prevent equine herpes I virus abortion. Normal but barren mares are put in winter quarters, allowed to exercise and maintained in a fair to good physical condition but should not be allowed to become too fat. The reproductive physiology of mares has been discussed in Chapter XII but a more detailed presentation of the clinical aspects follows.

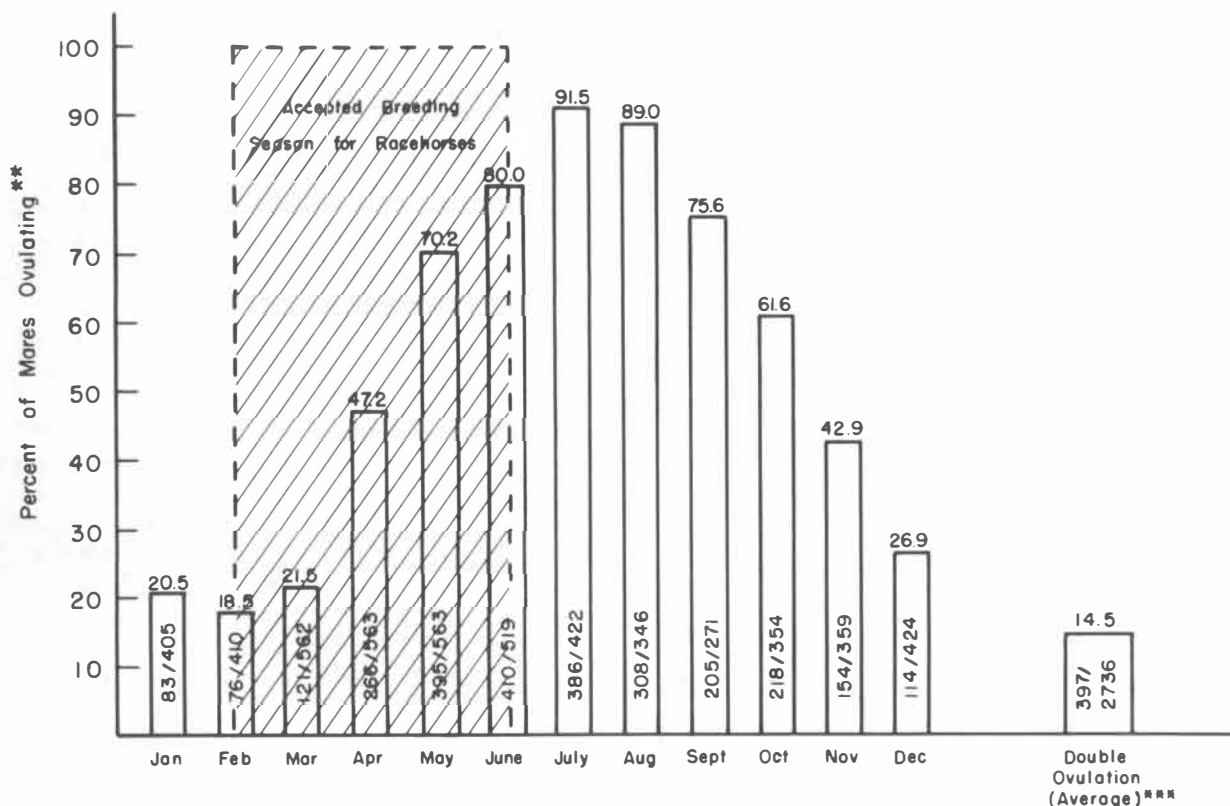
Reproductive Physiology of the Mare

Puberty in the female horse has been reviewed by Ginther¹¹⁵ (also see Chapter XII). By three months of

age the cortex of the ovary located beneath the fimbria completes its invagination into the medullary portion forming the ovulation fossa necessary to contain the large preovulatory follicles and to permit the fimbria to retrieve the released ova from the large equine ovary.³⁰² Between birth and about 4 months of age the equine ovary changes from the large oval shape of the fetal gonad to the adult bean-shaped ovary with a definite fossa. Ovarian follicles and occasional luteal bodies were observed between 6 and 9 months of age but evidence of ovulation was lacking. By 10 to 18 months of age well-nourished fillies reach puberty and develop a normal estrous cycle and ovulate. Of 137 yearling fillies run with stallions in small groups, 95 or 69% became pregnant. However 44 or 46% of these pregnant fillies aborted spontaneously between 30 and 160 days of gestation.¹⁹⁶ The high incidence of early pregnancy loss in these pubertal fillies was probably due to immaturity, inadequate nutrition, stress and possibly inadequate levels of progesterone.

The Breeding Season—In the northern hemisphere the breeding season of mares normally extends from March to October with the greatest degree of functional activity in May, June, July and August.¹⁵⁷ In data transposed from Australia to the northern hemisphere estrous cycles and ovulation occurred in June through August in 80 to 90 percent of 6763 equine genital tracts examined at slaughter by Osborne.²¹¹ During the winter months of December through March cycling and ovulation occurred in 18.5 to 26.9 percent of the 6763 mares' genital tracts examined and in 16 to 63 percent of the 792 mares' tracts examined in England.^{1,11} Thus some mares if fed adequately and housed will have regular estrous cycles throughout the year but there is a natural and common anestrous period from November to April for ponies and most mares, especially those on pasture (see Table 21).^{115,157,211} The horse being a photoperiodic animal with a breeding season regulated physiologically by the length of daylight has the lowest incidence of estrous cycling, about 25%, in January and February after the winter solstice in late December in the northern hemisphere when the length of day is about 9-1/2 hours.¹⁵⁷ As the amount of daylight increases in the spring increasing numbers of mares pass through a transition stage and commence regular reproductive cycling which reaches a peak incidence of about 100 percent in late June, the summer solstice, or July when daylight lasts about 15-1/2 or 16 hours. Ovulation usually lags behind the occurrence of estrous cycling and results in lower conception rates due to failure of ovulation early in the breeding season. Also longer periods of estrus occur early in the breeding season, 7 to 14 days vs 5 to 6 days later in the breeding season.¹⁵⁷ The monthly conception rate therefore follows this same pattern. Thus the physiologic normal breeding season

Table 21. A Frequency Distribution Graph Representing the Monthly Percentage of Ovulation for 5198 Normal Mares in the Years of 1959–1965*



* Adapted to the northern hemisphere from data published by V.E. Osborne, Dept of Vet Med, Univ of Sidney, Australia. Immature and senile mares excluded (Austral Vet. J. 42, 1966, 149)

** As evidenced by the presence of corpora hemorrhagica or corpora lutea in the ovaries of mares examined at autopsy. These mares come from an area of eastern Australia between latitudes of 23° 5" and 35° 5" corresponding to Southern N. Car through the tip of Florida or the northern to southern borders of Texas

*** The range of monthly variation in double ovulation was 7.2 to 21.4 percent

begins in late April or May after the spring equinox and ends in late September or October after the fall equinox, while the "operational" breeding season for breeds recognizing January 1st as the universal birthdate of each year's foals usually starts February 15 and ends the first week in July thus accounting for the major cause of horse breeding problems.

The photoperiodic reproductive pattern in the horse, as in certain other animals, is regulated in a complex, and not completely understood manner by the effect of increasing or decreasing daylight perceived through the eyes and transmitted to the pineal body and hypothalamus.¹¹⁵ The former releases melatonin that interacts with the hypothalamus to release GnRH to raise the levels of FSH and LH and promote follicle development, estrus, ovulation and CL formation in the early spring or summer and reverses this process in the late fall and winter.

Mares with 3 types of seasonal anestrus have been described:¹¹⁵ those, especially ponies, with a clear-cut period of anestrus of 2 to 4 months duration during the winter, mares that have some cyclic activity of a very irregular nature during the winter season, and mares, about 20 to 25 percent, that have regular cycles the entire year,^{140,176,177} (See Normal & Abnormal Estrous Cycling).

In the northern hemisphere most barren and maiden mares pass through a "transition" period of erratic, abnormal, irregular, anovulatory but receptive estrous cycling usually in the months of March, April and early May, between the winter anestrus and the normal breeding season characterized by regular estrous cycles and ovulation from mid May through September.¹⁵⁷ Every spring horse breeders invariably complain about the cold, dark or overcast weather and lack of grass to explain the

apparent delay in onset of the mares' physiologic breeding season. This impatience is readily transferred or expressed to the veterinarian who is expected within a few days to "speed up" a physiologic process that usually requires weeks to bring about. **The estrous cycle in the normal mare** is 19 to 23, average 21 to 22, days.^{7,16,17,18,115,239,261} The duration of diestrus averages 15 days but the duration of estrus was more variable, 2 to 11 days, with an average of 5.5 to 8 days. Breeding has no effect on the length of heat or the time of ovulation. Foaling mares usually come into their first estrum or foaling heat and ovulate between 4 to 18 days after parturition.^{239,269} In one series of cases 93 percent of the mares showed foal heat between 5 and 18 days and 77 percent showed foal heat between 7 to 10 days after parturition.²⁸⁵ Ovulation may occur from days 4 to 18 postpartum.²³⁹ Most foaling mares have normal or regular estrous cycles. A few may exhibit a prolonged foal estrum and a few more may fail to show estrus and exhibit anestrus for a variable or long period, sometimes called "lactational" anestrus. Often these anestrus foaling mares had a history of this pattern of behavior as a barren mare; this may simulate lactational anestrus in sows, or this may be seen in nervous overly-protective mares that fight the advances of the stallion approaching them and their foals.

The estrous cycles and estrous signs, and ovulation were very irregular, but ovulation did occur in female mules.⁴² In 47 pairs of mule ovaries atretic follicles were found in 12 and corpora lutea were present in 15 of the 94 ovaries. Female mules were infertile and primordial follicles in the ovary were rare.

The uterine endometrium did not return to its normal state by 10 days post-partum. But complete recovery did occur between days 13 and 25.⁷ Some mares had follicles on the ovaries one day postpartum and all mares had palpable follicles by day 5 postpartum.¹⁸¹ Four mares were in estrum to the teaser on days 6, 6, 7 and 8 postpartum and ovulated on postpartum days 7, 7, 10 and 14, respectively. Thus a short estrous period occurred in 3 of the 4 mares. In other mares the postpartum interval to the first estrus was 7 to 12 days in 7 of 9 mares and the duration of estrus was 2 to 3 days in 4 of the 7 mares. Further study is needed on the involution of the uterus and ovarian activity in the postpartum period of the mare.

Breeding on foal heat is generally contraindicated in mares that had an abnormal parturition with dystocia, a stillbirth, retained placenta, a placenta that weighed more than 14 pounds, or any contusions, or lacerations of the birth canal. As in cows nearly 100 percent of mares have a contaminated or infected uterus after foaling. In healthy normal mares this infection is eliminated early during

foal estrum. In 110 normal mares bred on foal heat only 43.7 percent conceived, while in 54 mares not bred on foal heat 67.3 percent conceived later on one service.^{18,151,285} The abortion rate in mares bred on the ninth day, or foal, heat was 12.8 percent, slightly greater than foaling mares not bred the ninth day. In another study of 304 mares bred on foal heat 39 percent conceived while 49 mares bred on the second post-foaling heat 55 percent conceived. The subsequent abortion rates and foaling rates of the two groups, even though rebreeding was necessary in each group, was nearly similar 16.5 and 13.8 percent and 66.4 and 66.2 percent, respectively.¹⁷³ In Kentucky 533 mares bred on foal heat had a 36.5 percent conception rate; 304 of these came back in heat and on the second service 56.6 percent conceived. Of 130 mares bred after 21 days following foaling, 58.5 percent conceived on first breeding.⁷⁵ Breeding on the foal estrum should be done advisedly, especially in old mares and in primipara.

The lowered conception rate on foal estrus may be due to breeding on a fixed date,^{183,218} such as the ninth day postpartum, instead of timing the service based on daily teasing and examination and manual palpation of the genital organs including possible culture. It is a common practice on many Standardbred and Quarterhorse farms to routinely breed all mares that foaled normally and had a normal postpartum period on the foal estrus even though it is generally recognized that conception rates at this period are lower than subsequent estrous periods. This is done to obtain the most foals from a band of mares each year and to avoid holding over until the following year a late foaling mare or a mare with a history of lactational anestrus as a barren mare. Furthermore most foaling mares are quite fertile and if they foal in February through April and conceive on foal heat, they are "out of the way" at the end of the breeding season in May and June when the stallion is being worked very heavily on mares that have foaled late or infertile mares that have failed to conceive. There is no evidence that mares that are bred on their foal heat and fail to conceive may have a reduced fertility at subsequent estrous periods.

Hormonal control of the estrous cycle has been reviewed and described.^{115,140,148} In the mare FSH is secreted in a periodic 10 day rhythm of surges, one in late estrus or early diestrus and the other in late diestrus, about days 8 to 12 of the cycle. There is evidence that these two surges of FSH per cycle, resulting in plasma levels of 10 to 15 and 20 to 25 ng/ml., respectively, may be reduced to one, the latter, late in the breeding season.¹¹⁵ Under the stimulus of FSH from the anterior pituitary gland follicles with an antrum are stimulated to grow.

Those follicles in the first "wave" become atretic about the middle of the estrous cycle because LH is not present to complete their growth, cause ovulation, and development of the CL. A nonsteroidal protein "inhibin" and estradiol present in follicular fluid suppresses FSH secretion and stimulates LH secretion. Waves of follicular growth and estradiol production occur every 10 days during the breeding season even though a corpus luteum may be present.^{115,149,261} Plasma levels of LH are high, 40 to 45 ng/ml. during the latter half of estrus and for several days after estrus and low from days 5 to 16 of the cycle.¹⁴¹ Progesterone concentrations in plasma are below 1 ng/ml. during estrus but rise rapidly after ovulation to a peak 6 days later of 6 to 10 ng/ml.

Regression of the CL around days 14 to 17 is due to a sharp rise in plasma levels of prostaglandins from the uterus, 60 to 240 pg/ml. The luteolysis caused by the uterine production of prostaglandins in the mare is accomplished by transfer of the prostaglandin through the systemic circulation to the ovary rather than the local utero-ovarian pathways described in the cow, sheep and pig. With follicular development estrogen levels increase a few days before estrus reaching a peak of 20 to 25 pg/ml. in plasma in mid-estrus several days before ovulation. Ovulation results from a complex series of biochemical reactions from progesterone and estrogens in the follicle, LH, cyclic AMP, prostaglandins and proteolytic enzymes.^{115,141} The hormonal levels and changes during the estrous cycle of the donkey have been described.²⁹⁰

Follicle development and ovulation—The size of the Graafian follicle ranges from 2 cm to 10 cm, or 0.75 to 5 inches or more in diameter, with amounts of fluid ranging from 6 to 112 ml. or more. Most follicles are 3.5 to 5.5 cm, 1-1/2 to 2 inches in diameter at the time of ovulation.^{115,239,261} Larger horses tend to have larger follicles. The follicular fluid during estrum contains estradiol-17B and estrone at levels of 48.0 ug and 3.4 ug per 100 ml., as well as a variety of other steroidal compounds.^{16,115,253} Almost all Graafian follicles are tense and firm on rectal palpation the first few days of estrum but within 16 to 24 hours of ovulation many follicles lose their tone and become softer and slightly fluctuating. It is possible they may already be losing some follicular fluid. The follicular fluid is probably a filtrate of blood plasma containing the steroid secretions of the theca interna.²⁵³ Urinary estrone varied from 15 to 20 ug per liter one week before ovulation to 60 ug per liter the day before ovulation.¹²⁹ Behavioral signs of estrus paralleled the urinary and plasma estrogen levels as did the changes in the genital tract associated with estrus. The major steroids secreted by the ovary were estradiol, progesterone,

estrone, androstenedione, a weak androgen, and other sex hormone steroids and their metabolites.^{239,253} Although the rate of exchange between the steroids in the follicular fluid and the blood were very slow, at the time of ovulation large amounts of estrogen were released.²⁵³ This may be related to the anticoagulant and enzymes in the follicular fluid. The size of the follicle is not related to sexual behavior but as the follicle increased in size during estrum, signs of estrus were more intense.⁷

The mature Graafian follicle is somewhat triangular or pear-shaped with the largest portion of the follicle palpable during estrus on the convex curvature of the ovary or at either pole of the ovary. The narrow stalk-like portion of the follicle protrudes toward the concave portion of the ovary or the ovulation fossa where ovulation invariably occurs in close proximity to the rather small fimbriated portion of the equine uterine tube. Only rarely does ovulation occur more than 2 cm. away from the ovulation fossa.^{9,11,12,38,210,225,226} Ovulation usually takes place toward the end of the estrous period, about 24 to 48 hours before signs of estrus cease; only occasionally is ovulation early or delayed so it occurs 48 to 96 hours before the end of estrus or 24 to 48 hours or more after the end of estrus.^{16,139,218} As described previously (see Abortion in Mares) double ovulation may occur in 4 to 40 percent, average 16 percent, of estrous cycles and only occasionally result in twin pregnancy due apparently to an efficient natural mechanism that eliminates one embryo early in gestation.^{115a,b} These double ovulations may be either synchronous, occurring within 48 hours; asynchronous, occurring 2 to 10 days apart, or be a single ovulation at estrus with a diestrus ovulation soon after the end of estrus. Ovulations without signs of estrus occur in about 24 percent of the diestrus periods of mares.^{138,139,289} Although equine follicular fluid has many properties of normal blood plasma it does not clot due to its having a lowered fibrinogen content and also to the presence of an anticoagulant heparinoid substance. This prevents the ovum from becoming trapped in a plasma clot.²⁶⁴ Since the mature follicle is highly vascular and the theca interna layer is hyperemic at ovulation, rupture of some vessels occur and clotting is delayed, hemorrhage occurring into the large cavity of the former follicle produces a soft, pulpy hematoma that can be palpated per rectum as a soft, mushy depression on the greater curvature of the ovary for 24 to 36 hours after ovulation.^{88,89,90b} The mare has by far the largest corpora hemorrhagica of all domestic animals.

The corpus luteum develops rapidly following ovulation and it also is triangular or pear-shaped. It occasionally protrudes as a button-like structure 1 to 2 cm. in diameter and 0.5 to 1 cm. in height beyond the ovar-

ian capsule through the ovulation site into the ovulation fossa where it may be palpated around the second day after ovulation.⁷ By 72 hours, range 1 to 6 days,^{115,130,132} after ovulation the corpus luteum, which is about 1.0 to 2.5 cm. in diameter, definitely smaller than the follicle, cannot be palpated readily unless the site of the recently ovulated follicle is known, because of the dense tunica albuginea and the central location of the corpus luteum in the mare's ovary. The corpus luteum actively secretes progesterone for 14 to 16 days when it begins to undergo involution or regression unless the animal is pregnant. Upon corpus luteum regression, follicle growth occurs under the influence of FSH released from the pituitary gland.

Fossa cysts or cysts of the germinal epithelium are common and may occasionally be palpated in the region of the ovulation fossa especially in older infertile or nonbred mares.^{8,186,187,210} These cysts were present in 64 percent of 42 ovaries.²¹³ These persistent small cysts could be single or multiple; they varied from 1 mm. or less up to 0.65 cm. and in rare cases could resemble a bunch of small grapes. These large accumulations might rarely interfere with the collection of the ovum by the fimbria at the time of ovulation. These cysts most commonly arise after an ovulation from the infolding of the epithelium, which is probably of paramesonephric origin, in the ovulation fossa region. These cysts are lined with ciliated columnar epithelium surrounded by a dense connective tissue layer. Fossa cysts resemble fimbrial cysts except for their location. There is no evidence that the contents of these small cysts have any hormonal activity.

As in other animals two to six or more follicles in two waves, early in estrus and at mid-estrus are stimulated to grow by the release of FSH from the equine anterior pituitary gland under the stimulus of GnRH from the hypothalamus. Ovulation occurs in one, or occasionally two, Graafian follicles under the stimulus of LH. Why some follicles develop and then become atretic and why one or two mature is not known.¹¹⁵ Irvine suggested that as soon as one follicle develops sufficiently to produce the inhibitor substance to lower FSH concentration in plasma the rest of the smaller follicles in the cohort become atretic.¹⁴⁸ Ovulation usually occurs from 1 to 24 hours apart in twin ovulations or synchronous ovulations. In some cases two or more days may elapse between ovulations in the same cycle or asynchronous ovulations.^{115,117b,218}

Fertilization occurs in the proximal end of the uterine tube. Unfertilized oocytes may remain in the tube for several months and degenerate before finally passing into the uterus. Thus the fertilized eggs can influence their own transport to the uterus probably by producing hu-

moral agents.^{41,115,239,294} Removal or loss of the cumulus cells occurs in the uterine tube.²⁶¹ The fertilized egg undergoes its first cleavage about 24 hours after ovulation and enters the uterus about 5 to 6 days after ovulation.^{115,239} Following ovulation the remaining follicles undergo atresia within 3 to 10 days.^{88,89} Mature follicles are highly vascular while atretic follicles become avascular and pale.

Since the duration of estrus is quite variable, generally longer in the Spring months and shorter in the Summer months, and variable between mares, determining the time of ovulation which usually occurs 24 to 48 hours before the end of estrus is difficult without repeated rectal palpation of the ovaries. Knowledge concerning the time of ovulation would be desirable so that copulation or insemination can be performed within 24 hours of the release of the egg.^{88,89,178,207} Of 353 mares 78 percent ovulated within 48 hours before the end of estrus. Nearly all of the remainder of the mares ovulated equally either 72 hours before or 24 hours after the end of estrus. Most mares are out of estrus within 48 hours after ovulation.

The administration of a luteinizing gonadotropic hormone, usually about 3000 IU HCG IM or IV, early in estrus, the first to third day, usually results in ovulation within 24 to 48 hours and a shortening of the estrus period one to three days.^{88,115,178} Ovulation occurred in 82 to 90 percent of the mares within 48 hours with three-quarters of them ovulating between 24 and 48 hours of the HCG injection. This HCG treatment did not adversely affect the conception rate.¹¹⁵

There is some evidence that repeated injections of HCG on successive estrous periods may be ineffective in reducing the interval to ovulation or the length of estrus possibly by the development of antibodies to HCG. Large doses of HCG may have an adverse effect on conception rates but further study is needed to verify this observation. GnRH has also been used in daily doses to promote the secretion of LH and hasten ovulation. Results to date have been inconsistent and further study on GnRH treatment protocols are indicated. GnRH could be used repeatedly in successive cycles without the production of antibodies that might affect the ovulatory response.^{115,149,309} After 2 to 5 injections of HCG, 2500 IU per cycle, 5 of 12 mares developed antibodies to HCG. The half-life of these antibodies varied from 30 to 60 days or more. No significant ovulatory refractoriness was observed in the mares.²³⁸ The use of HCG to hasten ovulation and shorten the estrous period is of value when it is desired to conserve the stallion by breeding a mare only once in an estrous period, to synchronize ovulations for AI or embryo transfer and to minimize trauma and infection in older "infection prone" mares or mares with

a Caslick operation or sutured vulva.

The time of survival of highly fertile equine spermatozoa in the genital tract of mares is up to 6 days.^{70,90a,115,261}

The survival time of less fertile semen may be shorter.

Sperm transport in mares is similar to that in cows, ewes and sows. When 7×10^9 spermatozoa were placed at the junction of the cervix and uterus during estrus only a very few, 0.06 to 2.2 percent, could be recovered from the genital tract 12 hours later. The uterus as in the other animals, is a hostile environment for spermatozoa. More spermatozoa from one stallion with the greatest sperm motility were found in the uterine tubes than from 2 other stallions, 17,000 vs 7,000 and 9,000 respectively.^{90a,214}

Whether copulation is performed 24, 48 or 72 hours before ovulation, conception rates are similar.^{88,90a} However, most veterinarians prefer to breed mares 12 to 24 hours before ovulation, especially if the stallion has a reduced fertility. No conceptions occurred in mares bred 2 to 4 hours after ovulation. Others have reported conception in mares bred 2 to 14 hours, and even to 36 hours after ovulation.^{16,28,32,115,135,239}

In the mare the sperm capacitation time in the female genital tract is short if indeed capacitation occurs in the horse.²⁵⁶ Thus if a mare is bred on the second day of the cycle and is still in estrum on the fifth day she probably should be rebred if she has not ovulated. With less fertile stallions more accurate timing of breeding in respect to ovulation will improve the conception rates. Where artificial insemination is employed mares are usually inseminated every 48 hours during estrus. In mares bred artificially at 48 and 72 hours intervals during estrus, the conception rates are similar.⁷⁹ Further studies are needed to accurately determine the survival time of spermatozoa and unfertilized ova in the mare's genital tract.

Equally good conception rates were obtained for breedings each of 4 days before ovulation.^{88,89,90a} The second to the fifth day before the end of estrus proved the most fertile time to breed to mare.²⁸⁵ To conserve stallions it was recommended that mares should be bred on the second or third day of estrum and teased daily thereafter. If they were still in estrum 4 days later they should be rebred.⁸⁴ Of 1187 mares bred, 80 percent had only 1 service per estrum and the overall percentage of pregnancies was 77.7. This method conserved the stallions and by reducing the number of copulations the dangers of establishing infection at the time of service were reduced. In a series of 1543 cases 2 or more services by a stallion during one estrum resulted in only a 3 percent higher conception rate than when there was a single service per estrum.²⁸⁵

Ovarian palpation—Usually four to six or more follicles can be palpated on the mare's ovaries during es-

trus. Because of the size of equine follicles especially the maturing or ovulating follicle, an erroneous diagnosis of "cystic follicles" or "nymphomania" may be made if they are compared to those in the bovine ovary. Follicles of various sizes and numbers are present on mares ovaries during the transitional or anovulatory periods in the Spring and Fall, or before and after the physiological breeding season, during all stages of the estrous cycle, including diestrus and during the first 4 months of gestation. Cystic ovarian disease as described in the cow does not occur in the mare.^{90b,152,186,187} "Persistent," or "autumn" or atretic follicles^{68,69} may remain in the ovaries for several months late in the fall. All follicles in mares that don't ovulate become atretic and involute usually by the next estrous period. Ovulation can occur in the mare when the reproductive tract is under progestational influences such as during diestrus,²⁸⁹ with a persistent CL and possibly during the first trimester of pregnancy. This has not been reported in the other domestic animals. One case was cited in which a non-pregnant mare with an active corpus luteum as revealed by plasma progesterone levels of 3 to 7 ug/ml. developed a follicle, was given HCG, bred artificially, conceived and delivered a live foal. Such mares with an active CL and follicle do not show behavioral signs of estrus.^{138,289}

Regular palpation per rectum of mare's ovaries during estrum has been practiced by some veterinarians to predict the time of ovulation, to detect the presence of two large or twin follicles and to determine when ovulation has occurred. The author and others^{115,239,261} have confirmed that prediction of the time of ovulation by daily ovarian palpation is not reliable and is highly subjective. The size of the maturing follicle is greatly variable from 0.75 cm to 7.5 cm or more. Changes in the consistency of the mature follicle as ovulation approaches is also variable. Most authors indicate that the follicle that is near ovulation becomes softer and less tense but this sign was observed in less than 30 percent of the follicles in one study²⁶¹ where daily palpation was performed and was not consistent in another where palpation was done every 12 hours.^{114,115} Furthermore, following ovulation the follicular cavity usually fills slowly with blood forming the corpus hemorrhagicum before the next palpation and can easily be mistaken for an unruptured follicle. Both the equine Graafian follicle and corpus hemorrhagicum are the largest of domestic animals.

In a study in which daily rectal palpations were performed during estrus, first cycle pregnancy rates were significantly lower in the treated mares than in the non-palpated control mares, 46 vs 79%, respectively. In a subsequent study palpation of mares every 48 hours during estrus only resulted in about a 10 percent reduction

in pregnancy rates compared to non-palpated control mares.^{297,298} The adverse effect of palpation on fertility occurred during or shortly after estrus, and may be due to an alteration of embryo transport in the uterine tube. During estrus in mares excessive palpation or palpation by inexperienced persons should be avoided.^{297,298}

Twin ovulations were highest during the summer months with a yearly incidence of 14.5 and 18.5 percent.²¹¹ Arthur reported a few cases of triplet ovulations and an incidence of 33.7 to 37.5 percent double ovulations in the summer months.^{9,11,12} He also noted the incidence of twin births to be 1 to 1.5 percent indicating a high early embryonic and fetal death loss in twin conceptions. Other authors have reviewed and reported similar findings.^{115,116,117,140,235} This great loss of early twin embryos may be a more important cause of infertility than is generally recognized. Twin or double ovulations are usually nearly synchronous as in 83 multiple ovulations 75 percent occurred within 24 hours and 90 percent within 48 hours of each other.²⁶¹ Twin ovulation in ponies is rare.¹¹⁵ Asynchronous double ovulations, with one occurring late in estrus and another 2 to 12 days later during the luteal phase of the cycle are uncommon, probably occurring in about 25 percent of the cycles.^{115b,116,117,261,289} Most twin pregnancies are the result of double ovulation but rarely identical twins are observed in a single allantochorion.²³⁷ About 52 to 60 percent of the ovulations occurred on the left ovary.^{7,9,211} As mentioned previously slightly more pregnancies occur in the right uterine horn than in the left uterine horn indicating that transuterine migration of the zygote in mares is common. A review of transuterine migration of the spherical early conceptus showed that about 50 percent migrated from the side of ovulation to the opposite horn early, 20 to 70 days, in pregnancy. Migration after day 40 is probably uncommon.¹¹⁵

Failure of ovulation or delayed ovulation in mares has been described.^{12,87,88,90b,129,218,295} It may be noted by repeated rectal palpation of the ovaries and is seen in mares early or late in the breeding season when cycles are often irregular. In failure of ovulation the Graafian follicle will become atretic and regress in 10 or more days and if this occurs in the Fall the mare may go into anestrus. In the spring of the year regression of the first follicle may occur to be followed in several weeks by a normal estrous period, ovulation and the commencement of regular cycles. Diagnosis of delayed ovulation or anovulation is difficult and subject to error unless the ovaries are palpated frequently by a skilled examiner. Clinically if this condition was suspected an injection of HCG, 1500 and 3000 IU, might be indicated to produce ovulation of a large follicle during estrus within 24 to 48 hours. Ovu-

latory failure during the estrous periods occurring during the physiologic breeding season is probably rare, 1 in 300 periods.²⁶¹

Infertility in Mares Due to Abnormalities of the Estrous Cycle: Their Recognition and Treatment

Abnormalities of the estrous cycle of mares, maiden, barren and foaling, is the most common cause of equine infertility or delayed conception.^{75,115,239} The abnormalities or irregularities of the mare's estrous cycle are closely associated with seasonal changes in length of daylight, nutrition, climate, or ambient temperature, "social" interactions or degree of stimulus by a stallion, and various stresses, including transportation and introduction into a new barn or environment, similar to those affecting the estrous cycle of sheep, goats and cats, the other photoperiodic animals.

Various routine, regular and common practices are followed on equine breeding farms to detect the stages of the estrous cycle, particularly estrus, where mares are "handbred" and not "pasture" bred. These practices include: teasing by a stallion, manual examination per rectum of the cervix, uterus and ovaries, and vaginal examination with a speculum of the cervix and vagina. Other less common examinations or tests might include hormonal assays, especially progesterone, on blood plasma or possible tests on vaginal mucus for the presence of elevated electrolytes during estrus by means of an instrument to measure electrical resistance.

Teasing or "trying" of mares by a stallion should be performed regularly on an every 24 or 48 hour, daily or alternate day, basis. During estrus teasing every day is desirable. All mares and stallions on the breeding farm should be carefully marked or identified by halter plates, hoof branding, or skin (freeze) branding. The clinical signs or behavior of the mare in estrus have been described^{7,17,40,110,115,239,261} as follows: the degree of resistance to the stallion decreases slightly 1 or 2 days before estrus. The greatest estrual response or receptivity to the stallion occurs 1 or 3 days before the end of estrus or just before ovulation. This is followed by a decrease in sexual desire for the next day or two before estrus ends. This increased receptivity noticed during estrus is probably related to and parallels the rise in plasma estrogen levels that causes the LH surge and ovulation late in estrus.^{115,239} However, the signs of estrus are not closely related to the plasma levels of steroids, estrogens or androgens. Mare with "silent" estrus may have the same levels as mares showing strong signs of es-

trus.^{201,239} Receptivity or acceptance of the advances of the stallion is usually characterized by the mare seeking out or associating with the stallion, swinging of the rear quarters toward the male, elevation of the tail, squatting or flexing the rear limbs, urinating small amounts of urine, and "winking" or rhythmic exposure or protrusion of the clitoris between the vulvar lips. This is caused by the contractions of the muscles at the base of the clitoris and in the perineum. The mare stands immobile and will allow the stallion to approach, sniff or nip her in the inguinal region, flank or buttocks and stand firmly to be mounted. Homosexual behavior such as mounting between females rarely occurs. When mares are not in estrus they violently resist the stallion's advances by laying their ears back, squealing and kicking at him.^{17,115,239} Some mares are phlegmatic or undemonstrative or impersonal before and after estrus or in diestrus and show neither much response nor resistance to the stallion. A few mares are always phlegmatic and never show external symptoms of estrus when teased. In these mares showing no receptivity toward the stallion at any time, the estrous cycle is nevertheless usually occurring, as evidenced by typical changes in the vagina, uterus, and ovaries and when adequately restrained such mares may passively or even actively, accept coitus with the stallion.

For a successful breeding program it is advisable and necessary to tease mares regularly in order to accustom them to the teasing procedure so they will not be frightened by confinement or by the teaser stallion's advances. Changes in their attitude toward the stallion can thus be accurately noted and estrus can be detected early. Teasing should be part of the daily routine and not performed before feeding or turning out and not performed outdoors in inclement weather. Some mares react promptly to the teaser while others must be gently teased for 5 or more minutes to develop their true reaction. On some farms a stallion is not available as a teaser and in these cases a gelding may be used. If he is too passive, injections of 250 mg. or more of testosterone, "Repositol" form, every 10 days to 3 weeks will usually make most geldings a satisfactory teaser. The masculine behavior usually disappears by 4 to 6 weeks after the last injection of testosterone. Detecting estrus in most mares is nearly impossible without regular teasing. Some may show signs of estrus when groomed about the rear quarters. Swelling, relaxation and edema of the vulva is slight but fairly common in mares in estrus. Regular examination of the vagina and external cervical os with a speculum or palpation of the cervix, uterus and ovaries per rectum by an experienced veterinarian can supplement or replace regular teasing of mares. Although these methods are

possibly more accurate than teasing in detecting true estrus and the time for service they are also more time consuming and costly under most situations.

Behavioral patterns during the estrous cycle including the submissive mouth clapping during estrus, have been described in the donkey.²⁹⁰

Teasing of the barren and maiden mare should begin 30 days or so before the breeding season or the date of desired breeding. This is done so that the mare will become accustomed to her surroundings, to the teasing stocks and the teaser, and not be frightened, excitable, or nervous when teased during the early part of the breeding season. These latter attitudes make it difficult for the handler, manager, or veterinarian to tell when estrus is present. This practice also acquaints the men observing the mare with her reactions toward the teaser stallion both in estrus and diestrus. This is of great importance in certain mares who do not show marked symptoms of receptivity or rejection toward the teaser.

The teasing stocks or bar is usually a solid partition about 5 feet high and 12 feet long often located about 3.5 feet from a solid wall, into which the mare is led and tied. No projecting posts or spaces between the boards should be present to cause injury to the mare or the teaser. The teaser is led up to the head and then the side of the mare and allowed to tease her. The mare's reactions are closely observed for signs of estrus or approaching estrus. A procedure that can be used where many mares are to be teased, as on a ranch, is to drive 10 or more mares in a long narrow chute and head the teaser stallion down the line of mares watching each mare's reaction.¹⁷ There are other techniques for teasing mares, including teasing of mares in their stalls by leading the stallion up to the door and if necessary backing the mare up to him. Mares teased in their stalls should be watched as the stallion enters the barn, as he teases them over the stall door, and after he leaves them. Some mares will "fight" or resist the teaser at their stall especially if they have a foal by their side, but will indicate estrus by relaxing the vulva and urinating after or before they are teased. A few managers tease their mares by leading the stallion through the pasture and circulating among them to determine their reaction toward the stallion. This requires an excellent and knowledgeable observer and it can be dangerous if a mare attacks the stallion. On other farms a Shetland or small pony stud is run continuously with the mares to detect estrus. Because of his small size he is unable to copulate with them. A surgical technique, to direct the penis of a teaser stallion to the rear so that copulation is impossible when he is placed with mares on pasture has been described.³⁰ A male pseudohermaphrodite with defective development of the penis could

also serve in a similar capacity. In range areas the stallion is often kept in a large stall or pen near the only source of water. The mares running in the adjacent corral or pasture can go to his pen when they are in estrum. This form of teasing only detects about 50 to 60 percent of mares in estrus.¹¹⁵

Teasing a foaling mare should be begun on the second or third day after foaling. The foal is usually left in the stall and watched so it can't injure itself, while the mare is led away to be teased, or if the mare objects too much a small box or pen in which to put the foal may be built in front of the teasing rack.⁷ A few mares fight or resist the teaser at all times even though in estrum. Some of these mares will show estrum promptly when a twitch is applied to their nose, thus distracting their attention so that their true reaction to the teaser is exhibited. Other mares have definite preferences in a teaser so teasing by 2 or more stallions may be desirable.¹⁰³ Occasionally a mare may show nearly typical heat one day and then not show it again. This symptom is observed most commonly in pregnant mares. Other mares are very phlegmatic and show little reaction to a teaser at any time. The use of a bold, aggressive teaser is very useful with these mares. Occasionally these phlegmatic, unresponsive mares come into estrum so gradually the casual observer might not notice it, but when they pass out of estrum the difference in their reaction to the teaser is usually observable. Then it is too late to breed the mare. Oftentimes a good teaser may recognize estrum in a mare and react accordingly with increased signs of libido, although the man observing the mare cannot see signs of it. Excessively fat mares may often be phlegmatic toward the teaser and fail to show estrum. The person who is responsible for the teasing of mares should be a keen and careful observer and accurately record his observations. The teaser on a large breeding farm is usually a stallion kept for that purpose or one that is seldom used. On smaller farms where stallions are used sparingly the breeding stallion can act as a teaser. Occasionally a "teaser" stallion may lose interest and libido. Allowing him to tease and breed a mare usually restores his ability to tease mares properly.

Although it is not frequently performed except on well-managed farms with a resident or contract veterinarian, mares that show estrum to the teaser may be examined by speculum, and/or their ovaries examined per rectum, at least 12 to 24 hours before being bred to make sure they are actually in true estrum and that ovulation is approaching. Speculum examination causes ballooning of the vagina and within an hour or so of coitus may interfere with the proper deposition of the semen. Rectal examination just before a natural cover may dilate the

anus and favor false entry by the stallion. Both of these practices should be avoided just prior to service. All mares should be teased daily or every other day until they are bred the second or third day of estrum, and daily teasing should continue until the end of estrum. If the mare is still in estrum 2 or 3 days after service she is usually rebred that same estrum. For the next 2 weeks teasing is necessary only every third to fourth day, and then 2 weeks after breeding teasing should begin at daily or every-other-day intervals. If estrum does not recur, teasing every third to fourth day may be continued for several weeks more and a pregnancy examination should be made. If a pregnancy examination is not performed by a veterinarian about 30 to 40 days after service, regular teasing every third to fourth day should continue during the breeding season, inasmuch as a few barren and foaling mares may show marked irregularities in the estrous cycle or lose an early embryo or fetus. Of the three procedures used for determining the stage of the estrous cycle, the stage of estrum, the time of ovulation and the best time for service, the external manifestations of estrus of the mare in the presence of a teaser or stallion is the most variable and inaccurate but is the only method available for most horse owners. The speculum examination of the vagina and cervix, or "spec exam," is the next most accurate procedure when performed by a knowledgeable observer. There is danger of introducing infection into the genital tract if this is not done properly. The most accurate procedure is the rectal examination of the ovaries, cervix and uterus by a skilled, experienced veterinarian. Although each of these procedures is rather subjective when they are combined the conclusions or diagnosis is quite accurate especially if repeated examinations to note changes are made at short intervals of 24 to 72 hours.

The physical signs of estrum in the genital tract of mares are characterized on vaginal examination by congestion and hyperemia of the mucosa of the vulva, vagina and cervix that increase in intensity from proestrus to ovulation and then decrease to a pale, quiescent state during metestrus and diestrus. During estrum the mucosa is very pink, hyperemic, or congested. There is an increased secretion of vaginal mucus that makes the mucosa appear shiny and allows the vaginal speculum to slide or slip with ease over the mucous membrane. Most mares in estrum seldom object to, and will stand quietly for, the vaginal examination. In the mare the amount of mucus is greatest and its viscosity lowest during estrum. Seldom is mucus observed at the vulva of a mare in estrum as it is in the cow. Also excess mucus is seldom observed on the floor of the vagina unless infection is present. The cervix does not contain tubular

mucus glands that secrete copious amounts of mucus, as in the cow. In late metestrus, diestrus, and early proestrus the vaginal speculum on introduction slides over the mucosa with difficulty, since the mucus is scant, sticky, and dry. During gestation this mucus is copious, sticky and gummy. The cervix during proestrus and estrus gradually relaxes, becomes flaccid, edematous, and quite hyperemic until it is very relaxed, hyperemic and edematous at the time of ovulation. The cervix, during estrus, especially in older mares, does not protrude noticeably into the vaginal cavity but blends into the cranial ventral vaginal wall. During metestrus the cervix may be red and moist but has more tone.^{115,172,239} At the time of ovulation the cervix is usually relaxed sufficiently to readily admit 1 to 3 fingers of one's hand. The endometrium at the time of estrus in a mare is very edematous and appears as large parallel and scalloped, thickened folds when examined by an endo- or fiberoptic scope. The old belief that mares require an attendant to insert his arm into the vagina and dilate the cervix with the fingers or "open the mare" before breeding has no basis in fact, and is contraindicated because of the danger of introducing infection. Furthermore if this is done just prior to breeding, pneumovagina may result and this interferes with the normal drawing of the semen into the uterus at coitus. **During late metestrus and diestrus** the cervix is tightly closed, pale, white and dry, and the external os appears puckered. At this time the contracted cervix protrudes into the anterior vaginal cavity.

On rectal palpation during diestrus the cervix is tightly contracted and has a distinct outline and occasional follicles may be noted on the ovary. **During proestrus, into estrus**, there is a progressive relaxation of the cervix, its tonicity decreases and near ovulation it is difficult to define the cervix because of its edematous, relaxed and flaccid walls. **Rectal examination at estrus** will reveal follicles present on the ovaries. 8 to 9 follicles are produced each cycle; normally only one or occasionally two, enlarge, mature and ovulate and the rest become atretic and decrease in size.¹⁶ The ovaries in young mares 3 to 4 years old are largest. Often the ovary containing the Graafian follicle or recently ovulated follicle is somewhat sensitive on palpation per rectum. During estrus, different from the cow, the mare's uterus is rather flaccid, edematous and soft on rectal palpation compared to the pregnant mare's uterus which is usually tonic and tubular. The uterus during diestrus is fairly firm, thicker and less relaxed.^{115,239} Endometrial biopsies show definite morphologic changes between the estrogenic and luteal phases of the cycle.^{115,239}

The vaginal smear in the mare is indefinite and of no value in differentiating the various stages of estrous

cycle.^{16,207} The pH of vaginal mucus during estrus in the mare is 7.4. A recent limited study reported that the vaginal pH of mares dropped from 7.4 to 6.8 on the day of ovulation. Further studies should be made to confirm this observation.²²²

The electrolyte or sodium content of vaginal mucus increases during estrus. Several studies with an instrument (Ovumeter) to measure the electrical resistance of vaginal mucous electrolyte changes as a means of detecting estrus and ovulation were conducted.^{54,258} This technique was of value in only about 50 percent of the estrous cycles in predicting ovulation within 48 to 96 hours as noted by a decline in transmittance. Thus this instrument is of limited value in the mare. Palpation of the ovaries to detect the time of ovulation or the presence of two mature follicles has been discussed. The plasma levels of progesterone and estrogen and their assay during estrus, diestrus and pregnancy of mares have been noted in Chapters II, IV, XII and under hormonal control of the estrous cycle in this Chapter. When a stallion is not available for regular teasing nor an experienced veterinarian to routinely examine a mare such assays if done every 2 or 3 days could be helpful in determining the stages of the estrus cycle or persistence of the CL.

On well-managed and veterinary-supervised equine breeding farms a combination of regular careful, closely observed teasings by a skilled observer, rectal palpations and/or vaginal examinations by an experienced veterinarian and the careful complete permanent recording of all findings at each examination or breeding must be followed. Certain mares, especially barren, older or maiden mares have lower conception rates and should receive more careful scrutiny than foaling mares which usually have fairly regular estrous cycles and also have proven their fertility. Since most mares have similar patterns of behavior, estrous cycling and ovulatory patterns from year to year, these accurate, complete breeding and examination records are very helpful.

Abnormalities or Irregularities of the Estrous Cycles in Mares

Most non-foaling mares, especially pony mares and those kept out-of-doors in the late fall, winter and early spring in the temperate zones are in deep seasonal anestrus during most of this period with small, hard, inactive ovaries, a flaccid uterus and a pale relaxed, flaccid cervix that in occasional mares may be partially to fully dilated.^{115,129,139,140,157,239} The vagina and cervix on speculum examination are pale, white, dry and sticky with-

out much mucus. If mares are stabled and well-fed up to 20 to 25 percent may exhibit occasional or fairly regular estrous periods or cycles. The transitional periods of anovulatory receptivity at the beginning and end of this seasonal anestrous period occur over a period of about 2 months in the late fall and spring in northern latitudes.^{115,157,239} Since mares are not often bred in the fall, and early spring breeding is usually desired, the latter transitional period between February and April characterized by either anestrus, prolonged estrus, erratic follicular growth and ovulation or anovulation and other cyclic and reproductive irregularities is a cause of concern to owners, managers and veterinarians. It has been remarked that during this transitional period between winter anestrus and the physiological regular estrous cycles in the late spring and summer, "the only consistency in mares is their inconsistency." In earlier years,⁷⁵ before 1960 to 1970, careful, regular teasing, examination of the genital organs and breeding, some mares would conceive during this frustrating transitional period but for most mares waiting until the physiologic breeding season arrived in the late spring and summer was the only alternative. Although more nutritional studies on mares are needed it has been generally noted and accepted that mares in good health and not overly fat when fed a properly balanced ration and/or pasture in adequate amounts to cause a gradual weight gain hastened the onset of the physiologic breeding season. Also regular frequent teasing or close continuous contact with stallions during the spring apparently favors the onset of the regular breeding season as in ewes and sows.³¹ Further controlled studies are needed to confirm this observation.

About 25 years ago it was shown that artificially increasing the amount of exposure to light each day will hasten the onset of estrous cycles and the shedding of the winter hair coat of mares.^{68,177,207} But only within the last 15 years has this technique been used on a practical basis. In the U.S. this has been done largely on Standardbred farms where foals born in November and December are registered on January 1st as their official birth date. By gradually increasing the amount of exposure to light by 30 minutes per week starting on October 1st for Standardbreds and December 1st for Thoroughbreds, most mares will be cycling and ovulating normally within 60 to 90 days or when the total daily exposure to light reaches 15 to 16 hours. Exposure to continuous light for 24 hours per day was less effective in hastening the onset of the physiologic breeding season than 16 hours per day of natural and supplemental artificial light. Thus, this technique will induce the earlier attainment of a fertile breeding state. This is advantageous in the racing breeds because it results in earlier foals, better distribution of mares

served by the stallion and by a greater number of exposures of infertile mares to stallions during the breeding season. This is especially valuable in mares that normally fail to show estrus until late May or June. During the early breeding season under lights, the same erratic or irregular reproduction periods such as prolonged estrus, irregular estrus, and failure of ovulation occurs as it does at a later period in mares not under lights. It was demonstrated that a 200 or more watts non-frosted incandescent or fluorescent light bulbs that provided 2 to 7 foot candles of light, 5–12 feet above the floor were satisfactory.^{176,177} If the mare is normal, artificial lighting should result in the conception of the mare in December through March or April, but if the mare is infertile for a variety of reasons, artificial lighting has no curative properties.^{80,115,157,239,250}

Gradually increasing light up to 16 hours per day or a constant 16 hours of light per day will result in the early induction of the physiological breeding season in mares. This artificial light regimen should be started in the fall October 1st through January 1st in the northern hemisphere. The lag time for follicular activity and ovulation with normal estrous cycles is about 60 to 90 days.^{115a} When this light regimen was started in October mares did not go into the seasonal anestrus period and came into regular cycling and ovulation by mid December or January.⁸⁰ It was also recommended that breeding stallions and teasers also be placed on this same regimen, because of the length of the spermatogenic cycle, about 60 days. Mares that foal prior to April 1st should also be placed on this regimen of 16 hours of daylight prior to foaling. After 5 years on this program 50 percent of the mares foaled from November through January compared to only 3.8 percent initially.⁸⁰ In another large study of Thoroughbred and Standardbred farms 50 percent of the mares under this lighting procedure foaled by March 31st compared to none on an unlighted control farm.^{176,177}

The transition from the anestrous state in to the breeding season whether artificially stimulated by lighting or occurring naturally is a gradual process characterized by certain definite changes especially in the ovaries as detected by palpation. The transition from "deep" anestrus, to "shallow" anestrus, and to estrus and regular estrous cycles with ovulation is characterized initially by an increase in size of the ovaries a number of days before follicles can be palpated.^{67,68,69} This is usually associated with a shedding of the winter hair coat, and an increased vascularity observable in the mucosa of the vagina and cervix. The ovaries feel spongy or rubbery compared to the firm fibrous ovaries of anestrus. In a few cases these mares will show estrus even though follicles cannot be palpated. Probably this is due to small follicles in the

ovarian substance that secrete estrogen. Then later in this transitional period due to artificial or natural light of about 16 hours duration per day and after irregular or prolonged estrus without ovulation, ovulation occurs with the commencement of regular estrous cycles.^{115,250} At the present time provision of artificial lighting, even with its long lag time is the most satisfactory and practical procedure for hastening or prolonging the normal physiologic breeding season in mares.

Hormonal methods, as in ewes, have been attempted to bring mares into regular estrous cycles during the winter anestrus period. Trials and studies have been conducted with progesterone, GnRH, equine pituitary extracts high in FSH and HCG and various combinations of these hormones with limited and inconsistent results.^{115,157,239,261} Further studies are indicated. HCG in doses of 1500 to 3000 IU, as discussed previously, induces ovulation within 24 to 48 hours in Graafian follicles capable of ovulating. Thus this reduces the duration of estrus and extra services by the stallion.

Progesterone treatment, 100 mg of progesterone in oil IM daily for 7 to 10 days, given late in the spring transitional season or early breeding season before regular physiologic estrous cycles and ovulation have been established have, in limited trials and in the author's experience, been quite effective in producing a normal estrous cycle within 3 to 5 days after the cessation of treatment with ovulation about 8 days after treatment.^{140,157,293} Normal cycles usually result thereafter with conception rates of about 50 percent on this first service. This procedure by its nature is limited to individuals or small groups of mares. Since the presence of definite follicular activity is necessary, this treatment does not significantly hasten the onset of the physiologic breeding season but it does appear to have promise in the treatment and control of the common irregular, prolonged estrous periods in non-foaling mares that delay the onset of the physiologic breeding season. Further studies are indicated including the use of the orally active progestogen, allyl trenbolone.²⁶⁰

Other factors such as stabling and adequate nutritive intake also influence the time of onset of the physiologic breeding season of mares. Stabling by conserving energy, providing warmth and often light, especially in the early morning and late evening hours, has hastened the onset of the spring breeding season in mares. Early spring pasture if available, provides an excess of energy and protein and is often associated with a marked increase in estrous activity and ovulation in the temperate zones. Frequent or constant exposure to a stallion has also been reported to hasten the onset of the breeding season as in ewes and sows.³¹ However further controlled studies are

needed on this phenomena in mares since another similar study indicated only a small but not significant difference between pony mares penned with a stallion and control mares.¹¹⁴

Clinical signs of abnormal or irregular estrous cycles resulting in infertility in mares may be due to physiological, genetic, nutritional, managerial or pathological causes. They may be classified on signs of receptivity toward the stallion as either prolonged estrus or prolonged diestrus or anestrus. Ovulation may or may not occur in these conditions. Ovulation nearly always occurs, however, in mares with normal length estrous cycles and estrous periods.

Prolonged estrus or irregular prolonged periods of estrus including "split" estrus. The former periods of prolonged estrus or frequent irregular estrous periods are natural and are common, in up to 90% of maiden or barren mares in the late transitional period or early physiologic breeding season in the spring and in mares in which the breeding season was moved forward by the use of artificial light.^{75,115,250} These prolonged estrous periods ranged from 8 to 30 days, average 18 days.²⁵⁰ They have been occasionally reported as lasting up to 60 days or more,^{75,140} during which the mare shows receptivity toward the stallion at nearly all times. Later in the breeding season this prolonged receptivity ceases and a normal estrous cycle with ovulation is established. As foaling mares these mares with a history of prolonged estrum early in the breeding season usually have an excellent sexual rhythm, regular estrous cycles and good fertility.⁷⁵ In the latter uncommon condition, "split estrus" the mare is in estrus to the stallion for one or more days, out of estrus for one or more days, then back into estrus for several days. Ovulation may occur at this latter time. "Split" estrus may on occasions, be a psychic phenomena, especially in maiden mares, related to stress, improper teasing, transportation or other factors.

Treatment of the condition of prolonged or irregular estrous based on the response of the mare to the teaser is most easily accomplished in most mares by waiting a month or so until regular estrous cycles are established in the physiologic breeding season. However vaginal and rectal examinations of these mares every 48 to 72 hours may detect a normal physiologic estrus with a large follicle at which time possibly HCG and breeding might be indicated. Repeated breeding of mares during these prolonged receptive periods may be harmful to the mare and is wasteful of the stallion. Hormonal therapy that might be useful in this condition would be the administration of HCG, 1500 to 3000 IU, when a mature, large follicle was present with other changes in the genital organs indicative of a physiologic estrus. In this condition pro-

gesterone therapy, 100 or 200 mg in oil, daily for 7 days takes the mare out of her receptive state even though on examination of the genital tract no signs of physiologic estrus are present.^{157,293} An oral progestin, allyl trenbolone fed at a rate of 22 mg per day for 12 days to 500 kg mares effectively regulated estrual behavior early in the year and synchronized estrus in cycling mares and had no effect on subsequent fertility.²⁶⁰ In another trial this orally active progestin reduced the protracted period of estrus and follicular development that commonly precedes the first ovulation of the breeding season but did not hasten the onset of the ovulatory season.²⁸⁶ This product is not yet available commercially in the U.S. Usually these mares come into a normal estrus 3 to 5 days later and ovulate about the 8 days after the termination of the treatment. Normal fertility and conception occurs at this estrus and subsequent estrous periods that follow this establishment of regular estrous cycles. The use of artificial lighting as described previously hastens the onset of the physiologic breeding season so that this common phenomena of the late transitional period doesn't interfere with the advanced breeding season.

Psychologic or false estrus or receptivity may occur with inactive ovaries or ovaries with no or only slight follicular development and the genital tract is pale, inactive with a closed cervix, no edema and a sticky dry mucosa and the reproductive or estrous cycle is absent. Mares may infrequently exhibit psychologic signs of estrus at any stage of the estrous cycle other than estrus during the winter anestrus season and even pregnancy.

Prolonged periods of anestrus or diestrus are common in mares as a cause of infertility or delayed conception. This condition is characterized by long periods of non-receptivity toward a stallion and is caused by a variety of physiological or pathological, temporary or prolonged, entities.

Physiologic anestrus is observed during pregnancy and during the winter season in most, 75 to 85%, of mares. The mares ovaries are small and inactive from 150 days to term in pregnancy and in ponies and pastured or "roughed out" mares in the winter, November through February or March.^{115,158,239}

Spontaneous prolongation of luteal activity or persistence of the corpus luteum has been recently documented as a common phenomena in mares.^{115,139,140,239,262} It is the most common cause of anestrus during the physiologic breeding season. The period of anestrus or non-receptivity lasts for 1 to 3 months, average 60 days, and is characterized by a failure of estrus, good uterine tone, a tight, pale, dry cervix, and elevated plasma progesterone values of 1 to 5 ng/ml that also persists for the length of the anestrus period. This occurs in mares with

normal genital tracts and the cause of the condition is unknown but probably is associated with a failure of the release of prostaglandin from the uterine endometrium about day 12 to 14 of the estrous cycle. This condition of a persistence of the CL occurred most commonly during the summer or the physiologic or breeding season, but may occur at any season in mares of all ages. It could occur in mares that were bred but failed to conceive. But a diagnosis of embryonic death or resorption would be incorrect. Ovulation, but not receptivity, may occur during this condition and in one instance pregnancy resulted from artificial insemination just prior to ovulation.^{137-140,262}

Treatment of this condition of prolonged luteal activity characterized by anestrus is the injection of prostaglandin, 10 to 15 mg of PG F_{2a} (**Prostin**) or 250 to 500 ug of fluprostenol (**Estrumate**) or other prostaglandin analogue that produces luteolysis of the persistent CL. The time of ovulation after treatment with a prostaglandin may vary from 1 or 2 days to 9 days. If a large follicle 4+ cm. is present ovulation may occur promptly with a short period of receptivity. About two-thirds of the mares ovulate from 3 to 7 days, average 5 days, and in the remaining third the large follicle regresses and a new follicle forms and ovulates at 6 to 12 days, average 9 days. Mares with follicles smaller than 3.5 cm. ovulate about 5 to 9 days, average 7 days, post-treatment.¹⁴⁰ Prior to 4 to 5 days post ovulation neither prostaglandins nor douching of the uterus is effective in causing luteolysis as the young CL is refractory to prostaglandin.

Douching a mare with 500 ml. of sterile saline to which antibiotics or antiseptics have been added to prevent infection or endometritis after the fourth or fifth day post ovulation and during diestrus when the CL is mature was shown to rapidly release uterine prostaglandins and cause luteolysis.^{13,203,239} This treatment was not as reliable as an adequate dose of prostaglandin.¹⁷⁴ If this spontaneous prolongation of the CL is caused by a lack or deficiency of uterine prostaglandins then uterine douching would not be effective and there would be a possibility of introducing infection into the uterus. In a large study of anestrus mares treated with a saline douche or prostaglandin the return to estrus within 2 to 7 days and the pregnancy rate were 40 and 39 percent vs 63 and 55 percent, respectively, for the two treatments.¹⁷⁴ The technique of douching the uterus was described in the 2nd edition of this text, and omitted from this edition because it is outdated, not as effective and more hazardous than the injection of a prostaglandin.

Saline infusion of the uterus in 25 mares that were determined to be non-pregnant prior to 40 days postservice all returned to estrus within 2 to 4 days after treatment. If such mares were not infused this anestrus state,

probably due to early embryonic deaths, lasted to 80 days or more.²⁹² A similar luteolytic response in anestrus mares occurred when they were given 250 mg. of stilbestrol intramuscularly and the mares were bred by natural service on the induced estrus 24 hours later. Within 7 to 8 days many mares so handled came into a true standing estrus and ovulated, conception frequently occurred if they were bred in this "second" physiologic estrus.²¹⁸ It is possible that the old empiric technique of "opening up" the mare by the groom manipulating and dilating the cervix was based on the physiological effects and the induction of estrus by such an act. One study showed that uterine biopsy, uterine culture, or cervical dilation and possibly AI, embryo transfer, uterine infusions or fiberoptic examination of the uterus if performed on the fourth or fifth day after ovulation or later in diestrus could shorten the estrous cycle or interestrus period and lengthen the subsequent estrous period due to the luteolytic effect caused by releasing uterine prostaglandin and regressing the CL.¹⁴⁴ Uterine "curettage" in the barren or infertile mare by drawing the cervix posteriorly with forceps fastened just lateral to the external cervical os has been accomplished by gently scraping the endometrium of both uterine horns and body with a sterile 70 cm. curette. This was supposed to simulate the stimulating effect of infusing the uterus with saline.^{167,256} The indications for and the value of this empirical technique are questionable. Controlled experiments and studies have not been undertaken. From these types and kinds of therapy to correct anestrus one can deduce that any significant invasion of the cervix and uterus if a CL is present may cause luteolysis of the corpus luteum and produce estrus in 2 to 10 days. The suggestion has been proposed that such practices possibly introduce organisms into the uterus resulting in endometritis and prostaglandin release and an abbreviated estrous interval which is well documented as a sequel to acute uterine infections. (See Infections of the Mares' Genital Tract.) The use of estrogens to correct anestrus or cause luteal regression in the mare has proven to be of no or very questionable value. Estrogens given to mares with a mature corpus luteum prolongs its activity and is not luteolytic as it is in the cow.²⁰⁷

Anestrus due to abnormal behavior, psychological anestrus, "silent heat" or subestrus is noted in mares that fail to show receptivity toward a stallion even though the estrous cycle, follicle growth, ovulation and CL formation occur regularly.^{75,115,137,239} These mares may show external signs of estrus only occasionally even during the physiologic breeding season but when they do show estrus they ovulate. Foaling mares, especially nervous mares that show great concern for their foals, are quite prone

to show psychological anestrus for several months after foaling. This may be termed "**lactational anestrus**" but it is not a true lactational anestrus as seen in sows, ewes and cows nursing young.¹¹⁵ This apparent "lactational anestrus" may also occasionally be due to persistence of the CL. Nervous, shy maiden or foaling mares may represent up to 10 to 15 percent of mares on a farm in which inadequate teasing fails to elicit estrous signs in the normally cycling mares. Some of these very protective foaling mares fail to show estrus and breed while a foal is at their side, the so-called "every other year mares." Frequent persistent quiet teasing by a vigorous male, free access of mares in a paddock to a penned stallion or pasture breeding to a quiet stallion, or careful repeated rectal and vaginal examinations and breeding by artificial insemination might be considered. These mares, either nervous or phlegmatic types, if presented to a stallion for service or teasing at the time they are approaching ovulation and restrained by a twitch or possibly hobbles will often "break down" and show external signs of estrus and acceptance of the stallion.

Conversely, certain fat, phlegmatic "impersonal," quiet, undemonstrative mares may also have normal regular estrous cycles and ovulation detectable on rectal or vaginal examination but be unreceptive to teasing similar to the former nervous or shy mare. Treatment is similar. By the use of a vigorous aggressive stallion as a teaser, frequent teasing, pasture or paddock contact with a stallion will often elicit signs of receptivity. The use of hormones such as estrogens in this type of mare is of no value. Occasionally mares will be nonreceptive to one stallion and exhibit estrous signs to another. One controlled study¹²⁶ on restricting suckling of foals to 4, 1-hour periods per day had inconclusive results. However two mares with a history of failing to exhibit estrus while nursing ("lactational anestrus"), ovulated and were bred and one conceived. Restricted suckling did not impair foal growth and development but when mares were stressed in late gestation by restricting their nutritive intake the onset of foal estrus and ovulation was delayed. This delay was apparently prevented by restricting the suckling of foals, even though the treated mares were more active and lost more weight due to the enforced separation from their foals for long periods each day. All mares with normal or long postpartum intervals, 17 to 30 days, to foal estrus had low plasma progesterone levels, less than 1 ng/ml, until after they ovulated. Further studies on this postpartum period are indicated.¹¹⁵

Anestrus due to various pathologic conditions will be discussed in more detail later in this Chapter. These are pathologic conditions involving the uterus and ovaries or systemic diseases. They are usually characterized

by a failure to exhibit signs of estrus on teasing and can be detected by a careful physical examination or laboratory tests. The conditions resulting in anestrus include:

1. **Pyometra** in which chronic advanced endometritis has caused the loss of uterine endometrial cells capable of producing prostaglandins. Injection of prostaglandins may produce estrus by regression of the CL but anestrus usually recurs depending on the degree of uterine pathology. The prognosis is poor. With a lesser degree of metritis and uterine infection, mares often cycle regularly or occasionally have short 15 day cycles.¹⁴⁰
2. **Hysterectomy and ovariectomy** will cause anestrus. After hysterectomy the lifespan of the corpora lutea were 67 to 137 days and after their regression estrus and ovulation again occurred. These conditions are incurable and rare.
3. **Granulosa—theca cell tumors** are the most common ovarian tumor in the mare. These mares exhibit either anestrus, stallion-like behavior or continuous or intermittent estrous behavior. The opposite ovary from the affected ovary is usually small, firm and inactive. Removal of the diseased ovary is indicated.
4. **Gonadal dysgenesis** similar to Turner's syndrome in humans is seen occasionally. These mares usually have a 63, XO karyotype. In one study 21 of 32 mares with chromosomal disorders were of this type.^{133,140} The ovaries of these mares are very small, smooth and firm and follicles seldom develop because of a lack of germ cells. The uterus and cervix are usually flaccid and relaxed and signs of estrus are not exhibited. Cytogenetic studies of these mares are necessary for a definitive diagnosis. Any mare with very small, hypoplastic ovaries should be regarded as a possible mare with chromosomal abnormalities.
5. **Anestrus associated with emaciation** may also be seen in old mares with pituitary tumors, old debilitated mares with poor teeth, heavily parasitized mares, mares with a chronic debilitating disease or mares that have been nearly starved or underfed or overworked and are extremely thin. Mares stressed by heavy exercise and restricted rations may exhibit "deep" anestrus.²⁰⁸ In these conditions the ovaries are very small, hard and inactive, the uterus and cervix are flaccid and relaxed and no signs of estrus are exhibited. Correcting the disease condition and improving the ration will in time often overcome anestrus due to these causes.
6. **"Nymphomania"** is a rare psychotic condition in mares, characterized by long standing severe

aggression and viciousness toward other horses and man. It is probably often caused in nervous, aggressive, horses by cruelty, or even timidity, of an owner or handler. Once the psychosis is well established, ovariectomy often has little or no effect on the mares behavior. These mares usually cycle regularly during the physiologic breeding season but are dangerous to work with and react violently toward a teaser or breeding stallion. In the stable the severely affected mare is vicious and may kick, bite, "run over," intimidate or jam her handler against the wall.

She tends to squeal, kick, squirt urine, and switch her tail if handled about the rear parts. For these reasons many owners think they are in constant estrus and call them "nymphomaniacs." Two types, a mild and severe, have been described.¹⁰ The former responds to ovariectomy, the latter does not. In the former the mare is often normal and tractable except when in estrus. These attitudes may be related to the elaboration of estrogens, progesterone and even androgens in the ovary. However, they will not tolerate the approach of another horse, a teaser or stallion; nor will they stand to be covered. They are dangerous to examine per rectum. They are useless as riding or draft animals. Because of the long-standing nervous derangement in these neurotic, unstable individuals, the vicious tendencies are well-ingrained and recovery even after an ovariectomy seldom occurs unless a skilled and knowledgeable horseman will retrain the animal so that it behaves sufficiently well in competent hands to be useful. Relapses to a violent behavior are common. Most of these advanced and long-standing cases of nymphomania or neurotic behavior should be destroyed before they injure a person or another animal. About a 60 percent recovery rate occurred after ovariectomy. The other 40 percent were long-standing vicious mares and response was not achieved.^{34,127} In another study 10 mares with nymphomania and frequent estrus all responded after ovariectomy; while many of the 15 mares with an unmanageable temperament during both estrus and diestrus showed marked improvement after ovariectomy. In all 25 cases the ovaries were normal with evidence of regular cycling.²¹⁹

7. **Anestrus, pseudopregnancy, or "spurious conception"**^{2,3} usually, but not invariably, occurs when an equine pregnancy terminates spontaneously or is intentionally interrupted after the endometrial cups have developed at 38 to 40 days of gestation. The cups remain and continue to secrete

PMSG. In Thoroughbred mares anestrus with hard, inactive ovaries may persist until the endometrial cups involute 80 to 110 days after their formation. Prostaglandin injections are ineffective during this period. Pony mares with pseudopregnancy may return to estrus but the associated follicles don't ovulate but often luteinize during this period of irregular cycling.

8. Two commercially-available anabolic steroid preparations were injected intramuscularly every 3 weeks, starting in December, for a total of 5 injections into 12 to 18 month-old fillies. These injections suppressed estrus and ovulation in most of the fillies for two breeding seasons, resulted in enlargement of the clitoris that persisted in some fillies for six months and caused various forms of stallion-like behavior including mounting that lasted for several months following the treatment.^{258a} Thus anabolic steroids should not be used in mares intended for breeding purposes.

Estrus synchronization and synchronization of ovulation has been generally successful in other large species of domestic animals. In the mare this is more difficult because of the long estrous period and the variable time of ovulation. But it would be desirable for artificial insemination, embryo transfer, planned or "spaced" matings and the control of the time of postpartum ovulations.¹¹⁵ The ideal goal of synchronization would be to be bred at a certain time without the need to detect estrus or ovulation. This goal is apparently a distant one in mares.

The four methods of control of the mare's estrous cycle that are currently available are:¹¹⁵

1. use of artificial lighting to hasten the onset of the physiologic breeding season. No practical hormonal therapy is currently available to induce ovulation and conception during winter anestrus period in mares,
2. use of HCG, 1500 to 3000 IU, early in the estrous period to induce ovulation within 24 to 48 hours and shorten the estrous period has been well-established and has been discussed in this Chapter,
3. use of progesterone in oil, 100 to 200 mg, IM, or a progestin, allyl trenbolone, 22 mg orally²⁶⁰ daily for 7 to 20 days to prolong the luteal phase of the cycle by suppressing estrus and ovulation in normal cycling mares resulted in estrus in 2 to 7 days after the end of treatment and,
4. use of prostaglandins, PGF_{2a}, 10 mg, prostaglandin analogues (fluprostenol) 100 to 250 ug, parenterally after the fifth day of the cycle to terminate the luteal phase of the cycle by luteolysis, or regression of the CL, and produce estrus within 2

to 4 days. In some synchronization trials two injections of prostaglandin were given to mares about 14 days apart when the stage of the estrous cycle at the time of the first injection was not known.¹¹⁵

The above products had no effect on fertility and might be used in combinations such as progestins and HCG or prostaglandins and HCG to produce estrus during a certain short period and to cause ovulation within a few days, respectively. Ginther¹¹⁵ has discussed the problems of synchronization of estrus in mares as they relate to the breeding season, the estrous cycle, the breed differences, for example ponies vs horses, the long estrous period and the variations in ovulation time. However with careful monitoring by an owner and a veterinarian individual or small groups of mares might achieve a satisfactory synchronization of estrus, ovulation and conception.

In one synchronization trial¹⁴⁶ two injections of prostaglandin (PG) were given 116 mares in 3 groups 15 days apart. Two of these groups were given HCG, 5 days after the last prostaglandin injection and bred AI. One group was bred once 21 days and the second group twice 21 and 23 days after the first PG injection without heat detection. The third group of mares was not given HCG and bred every other day of estrus. The conception rates for the three groups of mares were 57, 59 and 72 percent, respectively. Mares returning to estrus were bred by natural cover the next estrus and 98 percent of all mares were pregnant within 5 weeks of the first injection of PG. In another similar experiment²⁹⁹ PGF_{2a} was given twice 14 days apart and one-half of the mares bred AI after HCG and the other half bred AI after GnRH analogue on the fifth day after the last injection of PGF_{2a}. Although 81 percent of the mares were in estrus within 6 days after the last PGF_{2a} injection, conception rates were only 25 to 40 percent compared to 67 percent in a group of untreated mares. The use of progesterone impregnated sponges to synchronize estrus in mares during the breeding season as reported in ewes was only successful in 6 of 11 mares. Furthermore the sponges adhered to the vaginal wall, were difficult to remove and severely irritated the vagina.⁹⁸ PMSG given several days before the removal of the sponges was ineffective in causing superovulation or increasing the estrous response.

As discussed earlier and subsequently in this Chapter breeding on foal heat or estrus between 7 and 12 days postpartum results in 11 to 20 percent lower conception rates^{18,115} and possibly higher pregnancy loss than breeding later on the second postpartum estrus. An important postpartum interval of about 20 days is lost by routinely breeding on the second estrus. Furthermore, some mares

may exhibit silent estrus or anestrus following the foal heat due to their protective nature toward the foal even though ovulatory cycles may be fairly regular. Of 57 foaling anestrous mares, 42 or 75 percent had been bred on their foal heat. So the belief that only mares not bred on their foal heat go into anestrus is erroneous.⁸⁴ Some of the mares bred on foal heat and showing anestrus conceived but aborted or resorbed an early embryo.^{18,234} However in general foaling mares have regular estrous and ovulatory cycles with foal heat occurring between 6 and 12 days postpartum and ovulation between 10 to 12 days. This short cycle is usually followed by a regular cycle of 21 days and the second estrus occurs between days 25 and 35 postpartum. About 10 percent of mares may not have their first heat until 14 or more days postpartum. In order to breed mares on the second estrus or ovulation postpartum and gain the benefits of a higher conception rate yet not lose a valuable 20 day period, prostaglandin can be injected into foaling mares about 7 days after the foal heat ovulation or about 20 days postpartum. In 44 mares so treated 95% showed estrus and 82% conceived. In 36 mares not showing foal heat and treated on day 20, 68% came into estrus and 79% conceived.²⁸³ Thus delaying breeding for 18 days greatly increased pregnancy rates. Further trials should be undertaken. Delaying foal heat ovulation by the daily injection of progesterone, 100 to 200 mg. did not consistently block or delay ovulation and did not depress fertility.¹⁸⁰

An important recent clinical trial⁵ with 61 Thoroughbred mares in England illustrated the benefit of progesterone therapy at the end of the transition period and before the beginning of the regular cycling or breeding season during the months of February through May where no artificial lighting was utilized, as well as after parturition in mares in "lactational" anestrus. Thirteen to 20 mares each in shallow anestrus or prolonged estrus just before the regular ovulatory season and mares showing no estrus within 35 days after foaling, with plasma progesterone levels less than 1 ng/ml, were given 30 mg. of allyl trenbolone (**Regumate**) for 10 to 15 days. All 46 mares were in estrus within 8 days and all but 2 (4.4%) ovulated by 18 days after the end of the treatment period.⁵ This confirms Van Niekerk's early studies that progesterone therapy hastened the onset of the true breeding season in mares by apparently releasing LH to cause follicle maturation and ovulation.²⁹⁸

Early spring breeding mares need a regressing CL to prevent a long shallow anestrous period and prolonged spring estrous periods. Of 12 mares in deep anestrus 6 did not respond to progesterone therapy in the above trial. Increasing light artificially to 16 hours daily and giving progesterone therapy in 8 to 10 weeks would be indi-

cated.⁵ In mares showing prolonged "lactational" anestrus with plasma progesterone levels greater than 1 ng/ml, prostaglandin injections would be indicated as these mares are probably exhibiting a prolonged diestrous period with a persistent CL.

Attempts at superovulation and producing ovulation in the seasonally anestrous mare have only had very limited success.^{148,166,308} Large doses of purified equine FSH given daily for nearly two weeks were necessary and the frequency and cost of treatment made these trials impractical, considering the poor results obtained.

Nutrition and Infertility in Mares

In the past 10 to 15 years much research, using modern methods, has occurred in field of nutrition in horses at Cornell, Ohio State and other universities and research centers.²⁴⁸ The pregnant mare should be kept on a maintenance ration in only moderate body condition until the ninth month of gestation when a modest increase in protein and TDN should be provided until foaling. The barren mare should be kept on a maintenance ration also. During the breeding season both barren and foaling, lactating mares should be in a positive energy balance and gaining weight slowly. The pregnant mare might need increasing nutritive levels the last few weeks before foaling, and then a rapid increase in TDN intake after foaling to realize the highest conception rates on foal heat. It is important that mares to be bred on their foal heat and for a month or more thereafter be placed on a high energy ration. This may cause a problem in some mares that milk heavily by causing scouring in the nursing foal 1 to 2 weeks after birth. The feed intake of the foal may have to be monitored and the mare milked out manually. Thin animals and animals losing weight rapidly, usually fail to cycle and ovulate normally. (See infertility due to nutrition in cattle.)

Racing mares in training may remain in true or "deep" anestrus, even in the breeding season, due to stress, overwork, adrenal insufficiency and a probable lack of energy or TDN.^{35,208} In the former report changing to a pelleted feed resulted in a resumption of ovarian activity.³⁵ A low level of nutritive feed intake has no effect on fertilization.^{33,292} No embryonic resorption took place in mares that conceived on a low nutritional plane and thereafter received supplemental feeding before 18 days after ovulation. Eight mares on a low plane of feeding and a low protein intake after 18 days of pregnancy had an early death and resorption of the embryo between 25 and 31 days after ovulation as determined by rectal palpation. Mares placed on the poor ration after they were

35 days pregnant maintained normal embryos.³³ Mares having early embryonic deaths usually came back into estrum 40 to 80 days after service. Mares being provided additional hay and grain did not have the early embryonic deaths. The observation was made that supplementation of the diet with vitamins A and E appeared to improve the conception rate. However, a more recent study indicated that supplementation of an adequate ration had no beneficial effects on reproduction in mares.^{265,296} A properly balanced ration with sufficient TDN, protein, minerals, vitamins, salt, and water should be provided together with exercise for the foaling and breeding mare.

Overly fat, obese mares on lush pasture often are reported to be poor breeders. Possibly the reason they are fat is that they are poor breeders and do not nurse or carry a foal to use up the excess TDN consumed. Some veterinarians have empirically used 1 gm. per 100 lbs. body weight of iodinated casein with a 3 percent thyroxine potency (**Protamone**) daily in the feed of these obese mares to cause loss of weight. These mares should have been reduced in weight sufficiently during the winter months by restricted feeding so that in the spring months they could be placed on a slowly rising plane of nutrition and a positive energy balance to promote the onset of a normal estrous cycle, ovulation and conception.

Genital Infections Causing Infertility in Mares

Etiology and Symptoms. Infectious venereal diseases, other than contagious equine metritis (CEM) due to *Hemophilus equigenitalis*, do not occur in horses in the United States. Presently vigorous control measures



Figure 145. Ovaries in a 5-Month-Old Equine Fetus. (Note their size in relation to that of the fetal kidney located between them.)

have eradicated this disease, as well as dourine, from the United States. Genital infections in mares arise basically from four conditions. These are 1) pneumovagina due to an abnormal conformation or injury to the vulva and perineal region, 2) a normal or pathological parturition, 3) introduction of pathogenic bacteria at the time of copulation particularly in mares with a lowered resistance to infection and 4) introduction of pathogenic organisms on hands, instruments, infusion or AI equipment.

The first and most common condition causing a genital infection is pneumovagina, "windsucking" or aspiration of air into the genital tract. The normal mare's vulva should be at an angle of about 80° to 90°, or nearly vertical. The lips of the vulva should be full, firm and evenly closed their entire length. Pneumovagina is predisposed by a conformation that includes a flat croup, elevated tail head, sunken anus, and small underdeveloped vulvar lips that are pulled nearly horizontal by a sunken anus (See Figure 146). It is also caused by lacerations, scarring, stretching, or tearing of the vulvar sphincter muscles or the vulva or perineal body at the time of foaling. The perineal body, perineal center, or perineum in the narrow sense, is the complex joining of muscles and fascia between the anus and vulva.¹²² Whether pneumovagina is caused by the conformation of the perineal region or due to injury to the vulva, it results in infection of the vagina, the cervix, and oftentimes of the uterus. The question has been raised,¹⁸² but not answered, whether the conformation of the perineal area, especially in Thoroughbreds, American Saddlebreds and those horses with a high tailhead and flat croup, is inherited and surgery commonly used to correct pneumovagina to get affected mares pregnant is not perpetuating or increasing the numbers of these abnormally conformed animals. The vulvar lips in these "windsucking" mares becomes atrophic, flaccid, rolled in, gaped, or are sunken just below the dorsal commissure, allowing contamination of the genital tract with feces, air, and contaminating organisms. Once pneumovagina develops, the habit of aspirating air into the vagina becomes confirmed and it will usually become progressively worse unless treated. This condition is seen more commonly in old and thin mares but may be found even in young thin nulliparous mares. Standardbred or Quarter horses with more sloping croups and a lower tailhead are less commonly affected. (See Figure 146.) The peculiar gurgling, sucking sounds and expulsive blowing sounds occurring in well-developed cases, especially at the time of urination or defecation or at the time the mare is exercised are characteristic. Pneumovagina is more common at the time of estrum.⁷⁵ In fact aspiration of air into the vagina

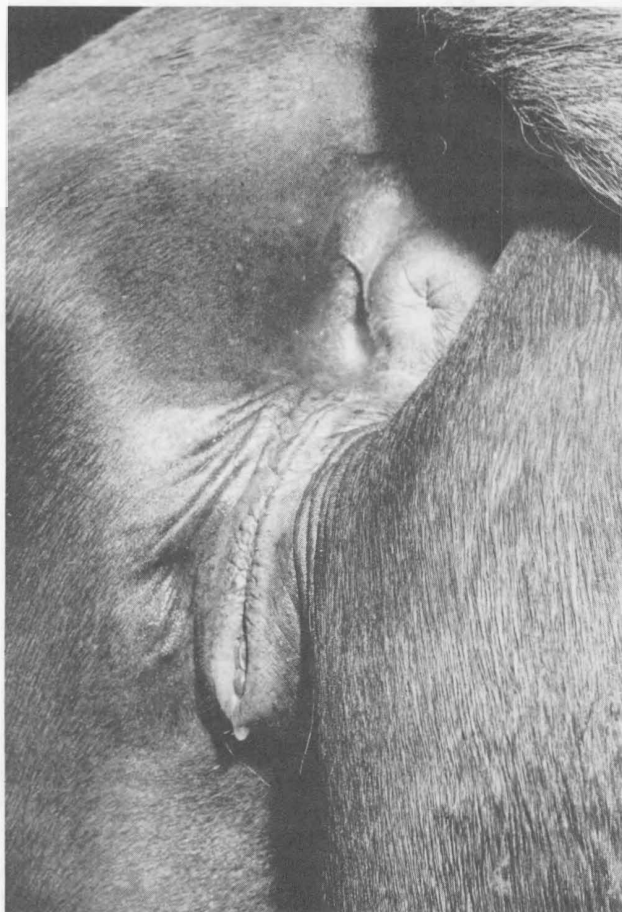


Figure 146. Appearance of the Perineal Region of a Mare with Pneumovagina. (Note the sunken anus, horizontal tipped vulva and the atrophic vulvar lips.)

may occur in some mares only during estrus. At this time the perineal region and the folds and sphincter between the vestibule and the vagina are more relaxed due to the influence of endogenous estrogens. Pneumovagina may occur in maiden mares in training, especially during the breeding season. The rare case of the outwardly-tipped vulva in maiden mares may also predispose to pneumovagina.⁷⁵ Pneumovagina may be a cause or a sequela of infection of the genital tract. In some mares the condition may be mild, infrequent and not suspected unless the mare fails to conceive and speculum examination or culture reveals evidence of a chronic infection of the genital tract. The presence of a small amount of foamy or frothy exudate in the vaginal cavity or a purulent discharge from the vulva about 5 days following coitus are almost pathognomonic symptoms of pneumovagina.⁷⁵ By introducing air and foreign material this condition may

involve not only the vagina but also the cervix and uterus. Many veterinarians^{75,96} have observed mares with definite symptoms of "genital windsucking" in which air and bubbles of vaginal exudate are sucked through the cervix resulting in ballooning and contamination of the uterus. Pneumovagina and pneumometra are associated with the reflex ballooning of the vagina and the development of a negative pressure in the uterus which occurs in the normal mare at coitus. These ballooned organs may readily be palpated on a rectal examination. Air does not normally gain access to the vagina and uterus at coitus when the vagina balloons, since the vulva is effectively closed by the penis.¹⁹³ The author has observed a few mares with only pneumovestibule. In these cases air is drawn into and expelled out of the vestibule causing a vestibulitis. The closure of the folds and the sphincter at the cranial or vaginal end of the vestibule apparently has effectively prevented the drawing of air into the vagina. This may be the initial state of pneumovagina. Measuring the length of the vulva from the dorsal commissure to the level of the pelvic brim in centimeters, the effective vulva length, and multiplying that by the angle of declination of the vulva gave a "Caslick Index" that could be related to the fertility of the mare.²¹⁵ Mares during estrus, with an effective length of vulva of 2 to 3 cm. rarely required suturing even as the vulva lengthens with age. Those with an effective vulva length of 5 to 9 cm. during estrus had a high Caslick Index and often required an operation at a young age. In this study 2110 mares (23%) had been operated upon; a low figure compared to about 30 percent of Thoroughbred broodmares in Australia upon which the operation had been performed.²¹⁵

The second source of genital infection in the mare is the normal and pathological parturition, characterized by dystocia, a dead or diseased foal, retained placenta, or severe trauma to the genital passages. Incomplete or delayed involution of the genital tract and uterine inertia following a pathological parturition has been stressed as a common cause of sterility.^{89,90b} The genital tract of all mares becomes infected during or just after parturition.^{58,59} This massive infection usually enters the genital tract when the mare rises soon after foaling and the vagina and uterus balloon with air. Cultures from mares the first 5 days postpartum invariably show bacterial growth but in normal healthy mares this infection is overcome or eliminated by the ninth or tenth day after parturition or sooner if foal estrus occurs early. It has been reported that the incidence of infections of the uterus and cervix at the onset of foal estrus can be greatly reduced by carefully washing and disinfecting the perineal region and rear parts of the mare before foaling, wrapping the tail in a sterile or plastic bandage, by allowing

the mare to foal on a sterile heavy rubber sheet covering the foaling stall floor, and temporarily closing the vulva with skin clips immediately after foaling.⁷³ Genital infections, injuries and lacerations following a pathological foaling, however, may cause pneumovagina which prevents the normal elimination of the infection.

Apparently the same but even more efficient mechanisms that eliminate infection at the time of estrus in cattle, sheep and swine are also operative at estrus in mares. This is an effect due to estrogens and other natural defense mechanisms causing a massive invasion of leucocytes, the "leucocytic tide," into the endometrium and lumen of the uterus to phagocytize and destroy infective organisms. The increased blood supply, mucus production, and the relaxation of the cervix all combine to rapidly restore the uterus to its nonpregnant, bacteriologically-sterile state in the healthy mare. This acute massive reaction to intrauterine infection also occurs at any stage of the estrous cycle and results in release of prostaglandins, luteolysis of the CL if it is present and the prompt onset of estrus with a shortened estrous cycle.^{134,137}

Thirdly, some cases of genital infection in mares may be due to infections introduced at the time of copulation from failure to observe hygienic procedures or by stallions that are carriers of a venereal infection such as *Hemophilus equigenitalis* (CEM), or possibly *Klebsiella* or *Pseudomonas*. Excessive frequency of breeding during an estrous period, especially in older, often infection-prone, mares should be avoided as it favors the establishment of a uterine infection. The mare that is to be bred should have her tail bandaged with clean, sterile gauze; the buttocks and perineal region and the wrinkles of the vulvar lips and skin should be thoroughly cleaned and washed with soap and water and wiped dry with pledgets of cotton to be certain that the perineal region is clean and free of dirt and epithelial debris. In a similar manner the stallion's penis and prepuce should be carefully washed with soap and water and rinsed both before and after service. If a mild antiseptic such as quaternary ammonium compound, chlorhexidine (Novalsan), or (Betadine) povidone iodine is used on the external genitals of the mare, the washed area should be rinsed with clear water before service. Excessive frequent use of such antiseptic solutions either on the mare or the stallion may result in a significant increase in *Pseudomonas*, *Klebsiella* and *E. coli* organisms, especially the former, that are resistant not only to the antiseptic solutions but also to antibiotics.^{51,202} Since the external genitals of the mare only require cleansing occasionally, excessive or frequent use of antiseptics should be avoided mainly in the stallion. The place in which

the mare is to be bred should be clean and free of dust and dirt and protected from wind that would blow dirt or chaff. Occasionally a mare will develop an acute endometritis after service due to *Str. zooepidemicus*, contagious equine metritis (CEM) organism or other infectious bacteria, these mares may have a short estrous cycle of about 12 days. These short cycles resemble those seen in cows with acute endometritis. It should be recognized that no matter how frequently or thoroughly the perineal region and vulva of the mare and the penis and prepuce of the stallion are washed and cleansed, a certain number of infectious organisms are going to be carried into the vagina and uterus by the penis and semen. The purpose of breeding hygiene is to minimize the numbers of organisms and the amount of foreign debris that are introduced. Because of the heavy bacterial flora in the sheath and on the vulvar lips, all semen, even that collected in a sterile artificial vagina, is usually fairly heavily seeded with a variety of organisms. If the accessory glands are infected then large numbers of infectious organisms will be in the semen and gain access to the uterus. Fortunately the normal protective mechanisms active at the time of estrus in most mares prevent these infectious organisms from becoming established in the mare's uterus and causing an endometritis and sterility.

A group of 97 mares free of genital infection was bred naturally. Careful and thorough breeding hygiene at the time of service was carried out. Twenty-four hours later a cervical culture of these mares was made. The incidence of infection in foaling mares, foaling mares bred on foal heat, barren mares and maiden mares was 90, 84, 87 and 81 percent. Six species of infectious bacteria and fungi were recovered. None of the above mares became chronically-infected following this natural service at the time of estrum.⁶¹

Fourthly, occasional carelessness on the part of the owner, handlers or veterinarians may introduce infection into the mare by means of improperly sterilized instruments such as speculums or douching equipment or contaminated gloves, sleeves or hands exposed to the genital tract of infected mares. Artificial insemination or impregnation may also result in the introduction of infection.

The Infectious Agents Causing Equine Endometritis and Infertility

A large number of infectious bacteria and fungi have been cultured from the genital tract of mares and stallions and on this basis have been reported to cause genital infections, endometritis and infertility or sterility. A

definite relationship between culture results and subsequent breeding performance has been demonstrated.^{20,77,101} In the latter study in New Zealand about 44 percent of mares with a positive culture produced a live foal while about 67 percent of mares that had negative cultures produced a live foal.¹⁰¹ Many of these organisms are commonly found in the external genital tract of mares, in the vulva and vagina, and in stallions on the penis and in the prepuce without producing an inflammatory reaction or disease. Thus positive cultures or contamination do not necessarily indicate active infection with a vaginitis, cervicitis and endometritis that could cause infertility. The wide variety and types of bacteria and occasionally fungi and yeasts that have been recovered from the genital tract of mares have not changed over the years,¹³⁷ except for the finding of *Hemophilus equigenitalis* as a cause of contagious equine metritis (CEM) in 1977.²⁷⁹⁻²⁸¹

The common organisms reported by Dimock and Edwards⁹⁷ and others^{20,77,137,144,230,234,239,252} include:

Hemophilus equigenitalis

***Streptococcus zooepidemicus* (genitalium)**

***Klebsiella aerogenes* (pneumoniae)**

Pseudomonas aeruginosa

Escherichia coli

***Staphylococcus aureus* and**

Enterobacter agglomerans

Other less common or miscellaneous organisms recovered from the normal or diseased genital tract of mares include: *Corynebacterium equi*, *Actinobacillus* (*Shigella*) *equuli*, *Aspergillus fumigatus*,^{48,144} *Candida albicans*, *Mucor* sp., micrococci, other streptococci, staphylococci, *Salmonella* sp.,¹⁷¹ mycoplasmas¹⁹⁸ and many others.

Other than a day or two after natural service or a few days after foaling when 80 to 100 percent of the mares are culturally positive, the highest reported incidence of bacterial infections based on culture occurs in barren mares, with foaling mares having a lower incidence and maiden mares the lowest, 20 to 45 percent, 14 to 20 percent and 5 to 10 percent, respectively. A total of 19 possibly pathogenic bacterial species were isolated from uterine swabs out of 498 (32%) of 1,539 barren mares over a recent 4-year period by 5 veterinarians.²⁵² Beta-hemolytic streptococci mainly *Streptococcus zooepidemicus* was isolated most commonly, 39 percent, while *E. coli* was found in 27 percent of the positive cultures and *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Staphylococcus aureus* in 7, 4.5 and 3 percent, respectively. Bacterial contamination was minimized by scrupulous attention to cleansing the external genitalia and perineum and in the handling of the culture speci-

men which was cultured by the veterinarian and sent in Amies transport media with charcoal to a diagnostic laboratory. The laboratory recovered and confirmed all but one of the positive cultures found by the veterinarians. Whereas of the total 81 samples cultured by both, 50 percent that were positive in the laboratory were not confirmed by the veterinarians. The normal healthy non-pregnant equine uterus, as in the cow, is free of infection. However a positive culture without clinical or histopathological signs of disease is of little significance and is often an inaccurate standard for measuring the status of the endometrium. In evaluating or interpreting the cultural findings a number of factors must be considered including: the mare's reproductive history, the age of the mare, the stage of the estrous cycle, the method used to obtain a culture, the site of the culture whether cervical or intrauterine or both, the degree of care used in cleansing and preparing the mare for taking the culture including the nature of the surroundings or location, the procedures and media used in inoculating, incubating, and identifying the cultures, or the media and transport techniques used in sending the cultures to a laboratory, and finally attempts by cytological or biopsy and histopathological examinations to determine the degree of endometritis and the possible pathogenicity of the recovered organism or its significance. Pure cultures of one organism in large numbers (many colonies on a plate) with evidence of endometritis is much more significant than mixed cultures of organisms or only a few isolated colonies with no evidence of the presence of many neutrophils.^{15,252} Furthermore if swabs are taken and placed in nutrient media that is not refrigerated or frozen, a few contaminant bacteria may multiply rapidly like in milk cultures for mastitis, so that those organisms overrun the culture plate and cause an erroneous diagnosis. When cultures are positive and no histological evidence of inflammation is present, the swab should be considered to be contaminated. Contamination of the swab before, during or after passage through the genital tract is an important factor in erroneous intrauterine swab culture results.⁴⁴ A completely guarded swab was superior to a partially guarded swab. However in this study, 63 percent of mares with histologic evidence of endometritis were negative on intrauterine culture.⁴⁴ When three sites, the vaginal fornix, the cervical os and the uterine lumen, were cultured at the same time on a large number of mares, there was only a 55 to 60 percent agreement on positive cultures between the various sites. A major pathogen was recovered from the uterus in 15 to 25 percent of the comparisons without being found at another site. Good correlation occurred in mares with a purulent uterine discharge.²⁰⁴ Although used for many years, un-

guarded cervical swab cultures taken visually using a vaginal speculum are not considered as satisfactory as the partially or completely guarded swabs for uterine culture.

Streptococcus zooepidemicus has been reported to be responsible for about 25 percent of the infertility in mares in Kentucky.⁹⁴⁻⁹⁷ This organism is a beta-hemolytic coccus that ferments lactose and sorbitol and belongs to the Lancefield Group C type of streptococcus. Besides being one of the most common causes of abortion and disease in foals it is the most common infection causing infertility. **Streptococcus zooepidemicus** is constantly present as a saprophyte on the external genitals of the mare and stallion and usually does not cause disease until the resistance of the genital mucosa is lowered by parturition, pneumovagina, breeding, old age, "wear and tear" changes in the endometrium, lowered resistance to infection and other unknown factors which allow the infection to become established.^{134,137,239} This lowering of resistance in susceptible or infection-prone mares is not due to a lack of immunoglobulins but is probably associated with a deficiency at the cellular level.^{14,112,134,137,220}

Nearly 100 percent of the mares have **Streptococcus zooepidemicus** as a contaminant of the genital tract for 3 to 6 days following parturition. Normal mares overcome this infection by 6 to 10 days following parturition, while other mares may not rid themselves of the infection until the second estrus or may remain chronically infected, especially if pneumovagina develops. Mild infection may not prevent conception but pregnancies in infected mares are likely to terminate in early embryonic death, abortion or a diseased foal. The incidence of early abortion, from 25 to 150 days, is greatly increased in mares with genital infections, especially streptococci.^{53,152} Most mares that have been sterile for 3 to 4 years usually have a pneumovagina and are infected with streptococci.^{89,90b} Often a spontaneous, persistent secondary infection with **Ps. aeruginosa** may follow these streptococcal infections.^{97,134} Infected mares are likely to exhibit a discharge from the genital tract. This exudate soils the vulva and perineal region including the buttocks and tail and the hair may become matted. The vulva may gape and the mucous membrane may be visible. Some cases show a marked loss of tone of the muscles and supporting structures of the vulva. The perineal region may be sunken. The vulvar lips are generally thin and atrophic. Examination of the genital tract will reveal a congested, inflamed mucous membrane. The cervix instead of being a pink color is more of a brick red to purple color with the cervical folds being edematous and the os relaxed and open. The mucous membrane is moist and the blood vessels are prominent, distended, and tor-

tuous. A thin, slightly cloudy mucropurulent exudate or a thick yellow-white exudate containing flakes of pus may be present in the vagina. Sometimes no exudate is found but in some cases a thin, clear, slightly frothy exudate may be seen coming from the cervix. These evidences of a vaginitis, cervicitis, and endometritis are most noticeable when the examination is made during estrus, since infected mares show a hypersecretion of mucus at that time. It may be difficult to distinguish between an acute and chronic infection, but the breeding history and the fact that old mares are more likely to be chronically infected may assist in the diagnosis. In chronic cases the exudate is mucopurulent and may be quite copious. In some advanced chronic cases, as pyometra, the uterus is dilated. The uterine wall may be atonic, and the mucopurulent exudate that accumulates cannot be readily expelled. In rare cases the uterine endometrium may be destroyed over extensive areas and be replaced by scar tissue. Evidence of pneumovagina is usually apparent.

Mild or recent cases require experience to detect or suspect on vaginal examination, as changes are not pronounced. For this and other reasons, many stallion owners require a health certificate on the mare before service. The certificate requires among other things a cultural examination of the cervix and/or uterus during estrus. As previously noted these cultural examinations require careful interpretation and accompanying clinical and histological examinations may be desirable.

Contagious equine metritis (CEM) is a recently-described, highly contagious venereal diseases of horses and donkeys. The causative agent of this disease is a microaerophilic coccobacillus organism, **Hemophilus equigenitalis**. It was first described in 1977 in outbreaks of the disease on stud farms in Great Britain and Ireland.^{12b,15b,23b} It has since been found in France, Belgium, Australia, Denmark, Austria, West Germany, Italy, Sweden, Japan and the U.S.^{8,66,109,113,131,159,223,224} In the latter country two outbreaks of the disease occurred in 1978 in Thoroughbred horses in Kentucky and in 1979 in Trakehner horses in Missouri. A small rapidly controlled outbreak occurred in Kentucky in 1982.³⁰⁶ Both former outbreaks in the U.S. were caused by infected, carrier stallions imported from Europe. On the two Kentucky farms where the disease was originally diagnosed, 412 mares were covered by 58 stallions. Based on cultures of the contagious equine metritis organism (CEMO) from the mare's genital tracts or the complement fixation test, 54 mares were infected. These mares had been covered by 16 stallions.^{65,66,131} The original source of the disease that appeared in England and Ireland in 1977 is unknown.

The causative organism, **Hemophilus equigenitalis** is

a Gram-negative nonmotile, short rod or coccobacillus that cannot be grown on conventional media but grows slowly on Eugon chocolate agar in 5 to 10 percent carbon dioxide at 37° C. Strains exist that are sensitive or resistant to streptomycin. Since media containing streptomycin inhibits the growth of contaminating organisms present on swabs from the genital tracts of mares and stallions and aids in the recovery of the CEMO resistant to streptomycin, it is necessary to also culture the swabs in media without streptomycin so the less common sensitive strains of CEMO can be recovered.^{113,245,274} There was no evidence of antigenic cross reactions of *H. equigenitalis* with other bacterial strains.²⁷⁴

Contagious equine metritis is clinically observable only in mares. The stallion is an inapparent or nonclinical chronic carrier of this infection on his penis or in the prepuce, urethral fossa, urethra and the urethral sinus or diverticulum in the glans penis dorsal to the urethra. Contagious equine metritis in the susceptible mare is usually characterized by the development of a profuse watery, mucopurulent, non-clumpy discharge or exudate associated with an endometritis, cervicitis and vaginitis within 2 to 12 days after service by an infected stallion. This exudate may drip from the vulva and mat the hair of the buttocks and tail. Short estrous cycles of 8 to 12 days are common during the acute stage of the disease. About 70 percent of susceptible mares bred to infected stallions show these typical signs.¹⁶⁰ Some mares may only exhibit the latter symptom with little or no vulvar discharge. CEM is characterized by a temporary infertility or failure of conception due to the acute endometritis following coitus. Irregular, long estrous cycles or early or late abortions have not been described in this disease. The CEMO may be transmitted from mare to mare by contaminated instruments, materials or personnel.^{8,66,113,131,223} There is no evidence the infection spreads directly from mare to mare. The mucopurulent discharge from the acutely infected mare contains large numbers of neutrophils containing many ingested organisms. No systemic signs of illness are observed. The genital discharge will last 10 to 20 days with clinical recoveries occurring without treatment. Both local and systemic defense mechanisms and antibodies are produced that assist in the rapid elimination of the uterine infection.^{65,113,131} Some infected mares will recover from the endometritis and conceive that breeding season. However, the level of conception and pregnancy may be reduced markedly to about 30 to 50 percent in acutely infected mares on a farm.¹³¹ In the initial English outbreak of CEM in Newmarket the percentages of "in-foal" mares dropped from 80 to 42 which, when combined with the cessation of breeding, resulted in an estimated loss of 30

million dollars.¹⁶⁰ Some of these mares that show spontaneous clinical recovery from the infection become carriers of *H. equigenitalis*. Besides these carrier broodmares and breeding stallions, teaser stallions may also be implicated in the spread of this organism on a farm.^{223,224} The carrier-state of mares and stallions may persist for months to a year or more and in the former may persist through a normal gestation period.^{8,66,131,223,224} In carrier mares the infection may occasionally persist in the pregnant uterus but most commonly persists in the clitoral fossa and sinuses which are homologues of their male counterparts, the glans penis, and the urethral fossa and sinus or diverticulum.^{161,255} These sinuses in the mare are usually three, or rarely more, in number located on the dorsal cranial aspect of the clitoral glans. They have narrow openings and contain varying amounts of greyish smegma-like material. The openings of these sinuses cannot be observed until the clitoris is extruded caudally and ventrally to pull the glans away from the thin fold of mucous membrane that separates the clitoral fossa from the vestibule. The central sinus is larger than the lateral sinuses. Heavy growths of CEMO and *Klebsiella* organisms have been obtained from the clitoral sinuses.²⁵⁵

The diagnosis of contagious equine metritis (CEM) is made on the profuse exudate developing a few days after service and the presence of many neutrophils in the exudate together with the finding of the Gram-negative intracellular and extracellular coccobacilli. Isolation and identification of the organism *H. equigenitalis* from the exudate is the only positive way to confirm the diagnosis. The isolation and identification of the organism is also the only procedure one can use to confirm the diagnoses of the infection in the stallion and the clinically-infected mare.^{8,66,113,131,159,223,224} In the stallion, sterile swabs soaked in sterile water or saline^{223,224} are taken for culture at weekly intervals for 3 or more weeks from the prepuce and penis, the urethra and the urethral fossa, around the end of the urethra, and the urethral sinus or diverticulum. In the mare sterile swabs are taken for culture from the cervix, clitoral fossa, clitoral sinus(es) and uterus, early in estrus^{245,246} and at weekly intervals for 3 or more weeks.⁸ In the pregnant mare swabs of the clitoral fossa and sinuses should be taken for culture. After the mare foals (or abortions) the placenta should be cultured as well as the prepuce, urethral diverticulum and penis of the newborn colt or the clitoral fossa and sinuses of the newborn filly, since occasionally CEMO are found in these sites.^{113,131,160,224,280} The latter sites on the newborn should be swabbed and cultured at weekly intervals on 3 or more occasions before the foals reach 3 months of age.^{109,131} Foals born of chronically-infected mares may

also be potential or possible long-term carriers of this organism and when bred the first time spread this infection to the stallion in the case of the infected filly or to the mare in the case of the infected stallion and thus initiate a new outbreak of this disease.¹⁶⁹ After foaling, and before breeding, the mare should be swabbed and cultured at 3 or more weekly intervals including once during early estrus. All swabs should be smeared on a sterile glass slide and placed in Amies media with charcoal or Stewart's media, refrigerated at 4 to 6° C and transported within 24 to 48 hours to an approved laboratory for the special culture and identification procedures necessary for this fastidious CEM organism. It was further recommended that on farms previously infected with CEM or others with much traffic from visiting mares that all stallions and teasers be swabbed and cultured twice at weekly intervals before the start of the breeding season.¹⁰⁹

After the outbreaks of CEM in other countries late in the 1970's the U.S. banned all imports of mares or stallions over 731 days of age from countries known to have the infection. In 1981 regulations were changed to permit older mares and stallions from these countries to enter the U.S. under quarantine and with certain restrictions including certified routine treatment and testing in the country of origin, similar to that required of animals after they arrive in the United States, with the last swabbing and culture within 30 days of the export date to the U.S. A clitoral sinusectomy is required in imported mares. After arrival in the U.S. horses are now consigned to an approved quarantine station in certain states with approved facilities where they are examined carefully to see if all the clitoral sinuses have been removed. If not, treatment is delayed and a quarantine imposed until proper surgery has been completed. The genital organs are then treated daily for 5 days. Seven days after treatment, routine weekly swabbings and cultures are conducted. Pregnant mares are examined and cultured, quarantined until foaling and then treated followed by routine weekly swabs and cultures starting 7 days after treatment.⁸ Stallions, especially those with streptomycin-sensitive CEMO, must be further tested after treatment, swabbing and culturing by breeding to two noninfected test mares. These mares are then cultured repeatedly on the 2nd, 4th and 7th days after coitus and again at the next estrus and two complement fixation tests are conducted 15 to 40 days after service at least 7 days apart.⁸ A possible supplemental test for suspect carriers of CEM was described that consisted of the infusing of smegma from stallions or mares diluted in sterile water into the uterus of a noninfected test mare. The contaminating bacteria were eliminated from the uterus of the estrous mare and the CEM or-

ganisms were recovered in pure culture from the uterus and cervix within 3 days. This technique was particularly useful when the CEMO was sensitive to the streptomycin used to control contaminants in the culture media. Also the CF test could be used 15 days after the inoculation to check for CEM antibodies.²⁷³ Specimens and all samples submitted to the laboratory must be documented and carefully identified.

Of the serologic tests available the complement fixation test is most sensitive and specific for detection of acutely infected mares from 15 to 40 days after the mare was initially infected. This test is of no value in the contaminated carrier stallions, chronic carrier mares, carrier foals or possibly pony mares.^{65,66,131,270}

Klebsiella pneumoniae var genitalium (formerly called Friedlander's bacillus or **Encapsulatus genitalium** or "viscid rod" infection) is observed much less commonly than **Streptococcus zooepidemicus** as a cause for mare sterility. *Klebsiella* infection is characterized by a thick, viscid, tenacious, slimy exudate that may contain flocculi.⁹⁷ The color of the exudate varies from dull-grey to yellowish-white. On speculum examination the vaginal and cervical mucous membrane is usually a dull reddish-brown color. During estrum exudation is profuse and may soil the vulva and tail and mat the hair of the tail and buttocks. These signs may develop within 2 to 7 days after infection and be able to be transmitted in a manner similar to a venereal infection, that is by a stallion or by contaminated equipment. This may be associated with certain highly pathogenic strains of *Klebsiella*.²³⁹ Following treatment the mare may remain a carrier as in CEM by the organism persisting in the clitoral fossa and sinuses. Since *Klebsiella* organisms are commonly found in sawdust and are a common cause of acute mastitis from that source in dairy cattle, the possibility of *Klebsiella* infection of the mare's genital tract from sawdust bedding should be considered. The presence of other infections tends to increase the inflammatory response of the genital tract to the *Klebsiella* infection. The inflammatory processes affect mainly the cervix and uterus and the principal changes are in the mucous membranes and the underlying structures. Often several hundred ml. of exudate is found in the uterus. On rectal examination the uterine wall feels thickened and the uterus is enlarged. If adhesions occur in the cervix, pyometra results; but these advanced lesions of genital infections are less likely to occur with *Klebsiella* infection than with the other types of organisms. The symptoms and lesions will vary depending upon the age of the mare, the length of time infection has been present, the time of the estrous cycle, the number and frequency of services during the breeding season. **Klebsiella pneumoniae var geni-**

Salmonella is a gram-negative encapsulated rod. It is readily transmitted from infected to healthy mares by the stallion at the time of service and by the hands or instruments of veterinarians or others who examine and treat mares. This infection is much more difficult to overcome than is the streptococcal infections and CEM. The sterility produced in chronic *Klebsiella* infections tends to be more lasting than in the streptococcal infections. This organism belongs to the *Klebsiella-aerogenes* group, and the paracolon bacteria, that are so difficult to treat even with antibiotics in cases of bovine mastitis.¹²³

Pseudomonas aeruginosa infection of mares' genital tracts was studied.^{135,137,239} Of 70 mares forty-two had a slight to definite hyperemia of the cervix and 15 mares had a milky-white exudate containing flocculent material that turned green, watery-grey, or yellowish-green on exposure to light. This exudate was noted from 6 to 38 days after service to an infected stallion.¹³⁷ *Pseudomonas* infection may spread to mares by stallions with normal conception rates. Older mares are more apt to develop endometritis and clinical signs of disease. Sporadic outbreaks of *Pseudomonas* infection may be caused by certain more pathogenic strains of the organism.²³⁹

The differential diagnosis of these and the other miscellaneous infections should be confirmed by bacteriological examination, as clinical symptoms are not sufficiently distinctive for an accurate determination of the etiologic agent. Routine cultures on suspicious mares should be made to confirm the diagnosis and on obviously infected mares to determine the etiologic agent and its sensitivity to antibiotics.^{227,228,239} Occasionally a mixed infection may be found on culture of the cervix. This is seen more commonly in pneumovagina. The genital tract of the normal mare, with the possible exception of the vulva, vestibule and caudal portion of the vagina, is free of infection or bacteria.²²⁰ A reliable culture may be obtained by culturing the cervix, or preferably the uterus during estrus since at other times of the cycle the diagnosis of infection in the tightly closed cervix causes some difficulties.

Other infectious organisms, especially *E. coli*, may be found on culture of the mare's cervix and uterus. The possibility of these coliform organisms, that grow rapidly on culture, being contaminants of the genital tract should be considered. Likewise fungi or yeasts may be found as contaminants but may rarely cause endometritis and even abortion. ***Candida albicans*** has been reported following prolonged antibiotic therapy of the uterus and vagina. To establish the diagnosis of a fungal or yeast endometritis it is necessary to culture the organism from the uterus, demonstrate the presence of endometritis and demonstrate the presence of the organism in the uterine

lumen or within the endometrium or endometrial glands.^{48,144} Thus to establish a diagnosis of a true uterine infection that could affect fertility the causative organism(s) must be found as well as clinical, cytological or histopathological evidence of an endometritis. The latter can be determined by a uterine biopsy. The procedures for taking endometrial biopsies and their evaluation will be described later in this Chapter.

The technique for culturing contagious equine metritis organisms^{44,169,170,205,239} (CEMO), *Klebsiella* and other organisms from the mare, is easiest while the mare is in estrus and the cervix relaxed and dilated. Swabs should be taken from the cervix or uterus and for CEMO and possibly other organisms, such as *Klebsiella*, from the urethra and clitoral fossa and sinus(es). The mare should be restrained, in favorable surroundings that are well-lighted, clean and free from dusts and drafts. Stocks, hobbles, a twitch, tranquilizers and extra trained help are often desirable. A new pair of disposable gloves should be worn for each mare. The tail should be bandaged with a 3 to 4 inch sterile gauze bandage or placed in a clean disposable plastic obstetric sleeve. The external genitalia should be carefully scrubbed, similar to a surgical site, with separate pledgets of cotton or gauze saturated with a disinfectant such as **Novalsan** (chlorhexidine) or **Betadine** surgical scrub working from the vulvar lips and opening and radiating outward until no soil is noted on the pledgets. The area should finally be dried with clean, moist pledgets to remove excess disinfectants.

Prepare the Tieglund* or similar guarded swab^{44,276} by removing the red plastic cap from the end of the plastic speculum or tube while still in the protective plastic envelope. The culture swab should be drawn into and protected by the tube or speculum. The opposite end of the envelope from the swab should be cut and the enclosed paper for identification should be shaken out. On the handle end of the swab place a pencilled circle next to the plastic tube or speculum. This mark indicates to the operator the distance the swab is passed and whether it is fully protected when removed from the mare.

Using an 8-inch sterile culture swab, the clitoral fossa is swabbed after spreading the vulvar lips with the cleaned gloved hand and exposing the clitoral fossa and sinus(es). A smear on a sterile glass slide is prepared and the tip of the swab is broken into the Amies transport media. A second 8-inch sterile culture swab is passed 1 to 2 inches into the urethra after locating the urethra with a clean gloved hand. A smear of the swab is prepared on

*Modified Tieglund Swab, Haver-Lockhart Laboratories, Shawnee, Kansas, 66201.

a sterile glass slide and the swab placed in transport media.

The prepared Tiegland or similar guarded swab is directed into the cervix or uterus, either with a disposable clean plastic sleeve on the operator's hand or with a sterile vaginal speculum.²⁷⁶ In the former preferred method, a disposable plastic sleeve is removed from a clean pack and drawn over the hand and arm without touching the outside to any contaminating object. Sterile lubricant is placed only on the back surface of the hand and the arm, not in the palm of the hand. The prepared open Tiegland tube or speculum with contained swab is placed in the palm of the gloved hand to protect it as the hand and tube with swab are passed into the vestibule and forward to the cervix. The tube or speculum is directed by a finger into and through the cervix and into the uterine body. The swab is pushed forward to the endometrium and moved back and forth and rotated. It is then withdrawn well back into tube or speculum as determined by the pencil mark on the shaft of the swab. The open end of the tube or speculum is returned into the palm of the hand and protected as it is removed from the genital tract. The swab is smeared on a sterile glass slide and the tip of the swab removed and placed in Amies media for transport.

In the double sterile glove or sleeve technique^{204,205} the culture tube containing the swab is placed alongside the index finger between a sterile glove and plastic sleeve, or two plastic sleeves, and carried to and through the cervix, even in diestrus. The tube containing the swab is forced through the index finger of the glove, the swab extruded and rotated and withdrawn back into the tube and guarded by the hand before the tube is removed from the genital tract. A smear is made on a sterile glass slide for staining and cytological examination and the swab placed in transport media along with proper identification and sent to the laboratory.

In the vaginal speculum method²³⁹ the sterile vaginal speculum is passed through the vagina and centered on and surrounding the cervix. However this technique may carry organisms from the vestibule to the region of the cervix. The open Tiegland or similar swab in its speculum is passed visually to the os of the cervix and into the cervical canal with gentle manipulation. The Tiegland speculum should not be forced through the cervix if it doesn't slip through easily. This is accomplished most readily during estrus. The swab is pushed forward 2 to 7 cm. into the cervix or uterus noting the pencil mark on the shaft to determine the depth of the passage of the swab. After moving the swab back and forth and rotating it, it is retracted well back into the speculum and the speculum and swab are withdrawn through the

vaginal speculum followed by withdrawal of the latter.

If abundant exudate is in the vagina, a sample should be aspirated with a sterile disposable plastic treatment pipette and syringe. Put about 5 ml. of the exudate in a sterile vial and chill immediately and keep refrigerated until it reaches a laboratory for culture.

The technique for culturing CEMO or other organisms from the stallion¹⁷⁰ is as follows. The stallion should be adequately restrained by a stallion shank, twitch and/or tranquilization or sedation. Teasing may be necessary for extension of the penis. The stallion should be approached on the left side with the handler on the same side staying close to the shoulder and girth area and forward from the rear leg. Using an 8-inch sterile swab, swab just inside the preputial orifice or if the penis is extended the reflected preputial membrane. Use another swab to swab the orifice and fossa of the urethra after grasping the extended penis with the hand caudal to the glans. While still holding the penis, a third swab is used to swab the urethral diverticulum or sinus. After collection, each swab should be smeared on a sterile glass slide and the swab broken and placed in a properly labelled vial of transport media, refrigerated and sent to an approved laboratory.

After washing the penis and prepuce with mild soap (Ivory) and water and rinsing with clean water and drying, pre-ejaculatory fluids may be collected in a sterile disposable beaker by proper teasing of the stallion. Five ml. of this fluid should be placed in a sterile vial and submitted with the above samples.

The procedures used to obtain satisfactory cultures of the uterine cavity and their interpretation have been discussed. Smears of swabs taken immediately after removal from the uterus are useful when stained, especially with Gram's stain, to determine the type of bacteria present and their numbers and also the presence of neutrophils and their number which is indicative of the degree of endometritis. Culture of this swab by the veterinarian and even sensitivity testing will give more prompt information than sending the culture sample to a laboratory in suitable media and under refrigeration. However a good diagnostic laboratory can provide more accurate information on the types of organisms and their sensitivity to antibiotics than can most field laboratories.

Endometritis due to the introduction of bacteria naturally at the time of service, at parturition or experimentally^{14,47,112,134,137,220} usually results in varying degrees of distention and turgidity of the uterus with an increased blood supply, enlargement, edema and relaxation of the cervix and a flow of flocculent pus and mucus through it into the vagina at any stage of the estrous cycle, luteal or estrogenic, in the young normal healthy

mare. A marked invasion of the endometrium and uterine lumen with many neutrophils rapidly phagocytize the infecting bacteria and eliminate the bacteria, especially streptococci, within 3 or 4 to 15 days with a return of the uterus to normal. Occasionally secondary infections due to organisms, such as *Pseudomonas*, may last through several estrous cycles before being eliminated by the well-developed defense mechanisms of the mare's uterus. These mechanisms include hormonal factors whereby estrogens cause a significant increase in phagocytic activity that enhanced the bacteriostatic uterine mechanisms while progesterone inhibited the immune response in ovariectomized mares.^{112,303} However in intact mares the endometritis produced by the infecting organisms caused the apparent release of prostaglandins from the endometrium and caused luteolysis of the CL with the prompt onset of estrous with a short estrous cycle. Immunoglobulins, based on a preliminary study, do not play a significant role in this uterine defense mechanism.¹⁴

Chronically infected, "infection-prone" mares with a chronic persisting endometritis or recurring endometritis are usually older, barren mares or mares with a poor reproductive history which when experimentally infected with bacteria into the uterus exhibit little if any reaction.^{134,137,220} The uterus doesn't become enlarged and turgid but the uterine lumen continues to contain a cream-colored exudate that may occasionally be noted in the cervix and vagina during estrus. Apparently the uterine defense mechanism in these mares is disrupted, probably at the cellular level, and the marked invasion of neutrophils and monocytes and the phagocytosis of the bacteria does not occur as in a normal healthy often younger mare.

Thus all degrees of endometritis may be observed from mild to severe, acute, subacute or chronic depending upon the pathogenicity of the organism, the numbers of organisms introduced into the uterus and the degree of resistance or ability of the uterine defense mechanisms to overcome the infection. Endometritis is a major cause of infertility in mares because of the resulting "hostile" environment for spermatozoa and the embryo. Cytological or histopathological examination may be required to detect endometritis as only 44 (39%) of 114 mares with endometritis showed significant bacteriologic findings on culture.²³⁹

Metritis and pyometra due to these same wound-infection type of organisms often results in rather pronounced pathological changes in the uterus especially in older "infection-prone" mares with defective uterine defense mechanisms.^{137,239} Deep red, hemorrhagic areas and intervening areas of whitish-yellow mucosa may be scat-

tered irregularly in the endometrium. In severe cases the endometrium may be denuded at many points and have a dull, red, granular appearance. The amount and consistency of exudate present may vary from less than 100 ml. to 5 to 10 gallons and from watery, to mucoid to inspissated or cheesy. In metritis, as in cervicitis and vaginitis, the changes, depending on the stage of the cycle, the type of organism, and the predisposing causes, vary from a mild superficial involvement of the endometrium or endometritis readily cured by proper treatment or sexual rest to severe, advanced, and permanent pathological lesions of the endometrium with small abscesses of the uterine glands and chronic fibrotic, degenerative and proliferative changes in the endometrium and uterine wall. In cases in which the cervix is closed by adhesions or induration the uterus may contain several quarts or gallons of mucus.¹⁸⁶ In this unusual type of pyometra, or uterine abscess, the endometrium may be severely degenerated and eroded and the mare is anestrus. The uterine wall may be thin and atonic and in advanced cases the endometrium is almost completely destroyed. The mucosa in some cases becomes a tough, thick, yellow-white fibrous pyogenic or diphtheritic membrane. In the occasional pyometra case due to subinvolution of the uterus with an open or patent cervix, the endometrial pathology is not so severe although edema, degeneration, desquamation and sloughing of small areas of the endometrium may occur. In these cases estrous cycling may result in evacuation of the mucus. Pyometra in the mare may be associated with a retained or persistent CL and failure of estrus up to 12 months or more as in the cow. If the endometrium is sufficiently diseased so that prostaglandin is not released to cause luteolysis, the progesterone levels remain above 2 ng/ml. in blood plasma. A neutropenia without a left shift and occasional lymphopenia with mild erythropoiesis and an increase in monocytes and eosinophiles have been reported in mares with pyometra.¹⁴²

In rare cases of pyometra, or of uterine abscess due to adhesions or obstructions in the cervix it may be necessary to break the adhesions or to make an incisions through them to release the pus. Placing a gauze pack or plastic pessary^{172,190} in the opening for several weeks will allow establishment of a fistulous opening for drainage into the vagina and prevent the uterus from refilling with pus. Prognosis for future breeding of such mares is poor. Successful removal of the uterus and ovaries, ovariectomy, in mares with severe pyometra or uterine abscess has been reported.^{195,307} In one case observed by the author nearly 15 gallons of pus were drained from the uterus of a small mare with cervical and vaginal atresia due to adhesions. The mare had suffered a severe

dystocia 6 months previously. Such mares are incurably sterile. Perimetritis in the mare is apparently very rare, or else when it does occur the results are fatal due to peritonitis. In severe chronic metritis, particularly due to *Klebsiella* infection, a typical chronic productive inflammation results that may produce an atrophy and fibrosis of the uterine wall from mucosa to serosa.

Cervicitis due to a variety of infections is common and injury to the cervical mucous membrane can occasionally be serious in nature. In cervicitis the mucosa as seen at the external os is usually congested and dark red to purple in color; the os is generally edematous, pendulous, and dilated. In rare cases the cervical glands become cystic; deep suppuration and abscess formation may occur. Fibrosis of the cervix is usually not as pronounced as it may appear clinically, nor as severe as in the cow with advanced cervicitis. The inflammatory process involves mainly the mucosa of the cervix. In rare cases membranous or solid, thick adhesions may completely obstruct the cervical lumen and since uterine infection is usually present, pyometra or uterine abscess is likely to develop. Severe lacerations, scarring, and malformation of the cervix may occasionally occur in the mare at the time of parturition and produce a chronic cervicitis or cause a failure of the normal closure of the cervix, or incompetency of the cervix, resulting in repeated early embryonic or fetal deaths due to recurring infection, endometritis and permanent sterility. The surgical repair of cervical lacerations resulting in an incompetent cervix performed a month after foaling during the diestrous period where after debridement, the cervical mucosa, the cervical muscle and the vaginal mucosa are sutured separately is described.¹⁰⁵ A simple retention or purse-string suture placed around the caudal portion of the incompetent cervix after breeding or early pregnancy diagnosis is also described.¹⁰⁵ This suture must be removed a few days before foaling. Repeating these surgical procedures is usually necessary after each foaling.

Vaginitis and vulvitis due to a variety of infections is commonly observed. The vagina and vestibule appear to be more resistant to irritation and permanent damage caused by infections than does the cervix and uterus. In severe metritis and cervicitis with a catarrhal exudate the vagina is usually involved. Mares that develop the habit of pneumovagina or pneumovestibule usually exhibit a vaginitis and vulvitis often with a mucopurulent exudate. Fecal material and urine may occasionally be found in the cranial part of the vagina. Injuries, trauma, lacerations, or severe infection of the vulva and vagina at parturition may cause chronic vaginitis, pneumovagina, and in rare instances stenosis of the vagina. A rectovaginal fistula causes a severe vaginitis. Occasionally the cloudy,

turbid, light-colored urine of the mare may be confused with a vaginal discharge by the owner. In rare instances cystitis in the mare may develop but is usually secondary to a vaginitis or metritis.

Urovagina, "urine-pooling" or vesicovaginal reflux in the fornix of the vagina is occasionally noted in barren, old, pluriparous mares with a large pendulous uterus, sunken anus and horizontal vulva that allows urine to flow into the cranial portion of the vagina especially during estrus. This condition is often associated with pneumovagina and sterility. A few cases may occur around foal estrus and as uterine involution progresses urovagina may terminate after 2 or 3 postpartum estrous cycles. In early cases of persistent "urine-pooling," carefully douching the vagina with several liters of sterile physiological saline solution to which antibiotics have been added and then removing the saline just before natural service or preferably A.I., followed promptly by the Caslick, vulva-suturing operation often results in conception. In long-standing cases or those in which vaginitis and endometritis are severe, vaginoplasty or urethral extension by surgery on the caudal vaginal floor and/or vestibule can be successfully performed to prevent urovagina.^{56,197,239,301} Caslick's operation is usually also performed on these mares.

Salpingitis is rare in the mare. An enlarged uterine tube was never found on rectal examination of the mare.⁹⁷ On postmortem examination of 83 mares with metritis, only 18, or 21.7 percent, showed evidence of salpingitis as determined by gross and microscopic examinations. Not all oviducts that showed inflammatory changes were positive on culture. Salpingitis in the mare is an ascending infection from an infected uterus. Some infected uterine tubes undergo no pathological changes while most others exhibit only a slight catarrhal inflammation. In very rare cases, inflammation may be severe enough to cause fibrosis and occlusion of the lumen with inflammatory exudates. In no cases were the uterine tubes thickened and enlarged. In 700 equine genital tracts examined in Belgium all were patent and cases of hydrosalpinx were not present.²⁸⁸ Two cases of hydrosalpinx and one occluded oviduct were reported by other authors. This latter condition was due to an oviductal cyst. However infundibular adhesions, infundibulitis, and ampullitis was commonly found in 40, 37 and 21 percent of the tracts, respectively. Endometritis was noted in 31 percent of the tracts and often associated with isthmitis that occurred in only 9 percent of the tracts. The cause of the infundibulitis was unknown but factors such as bleeding at the time of ovulation as occurs in cattle or possibly *Strongylus edentatus* larvae were suggested. The degree to which this common nonocclusive chronic

salpingitis reduces fertility is not known. A safe, reliable accurate means of checking the potency of equine uterine tubes by injecting starch granules on to the ovaries and finding them in the cervix one to 7 days later has been described.^{4,239} The presence of a papilla containing a smooth muscle sphincter through which the uterine tube opens into the uterine cavity may furnish a possible explanation of the rarity of severe salpingitis in the mare.

Ovaritis in the mare is very rare. Evidence of acute inflammation of the ovary was rare in any postmortem cases.^{1,50,97} Two cases of an ovarian abscess in which **Streptococcus zooepidemicus** was found in one were reported.^{50,97} One was secondary to the tapping of an ovarian cyst. Adhesions between the ovary and surrounding tissues is rare except in association with ovarian abscesses.

Prognosis of Genital Infections in Mares. Uterine, cervical and vaginal infections in mares due to pneumovagina or infection of the uterus after parturition, abortion or service usually respond to treatment. In many acute cases of endometritis in normal, healthy mares resistant to infection prompt recovery without treatment, except in cases of pneumovagina, may occur within several days or weeks as discussed previously. The sooner a persistent infection is diagnosed and the proper treatment given, the more favorable the prognosis. In long-standing, severe cases due to virulent pathogenic bacteria, endometrial damage may be severe and permanent and result in sterility. Massive purulent metritis with cicatrization causing a loss of endometrium, and extensive cervical lacerations are two conditions that may render a mare hopelessly sterile.²²⁷ Usually it is much more difficult and takes longer, and may occasionally be impossible to correct chronic infections due to **Ps. aeruginosa**, **E. coli** and **Klebsiella** than streptococcal and CEM infections, as the former organisms are more resistant to antibiotics and other treatments and cause greater tissue damage than the latter. In early mild infections proper treatment may result in prompt recovery within 1 to 2 months. In severe or chronic cases treatment and sexual rest for 6 months or more may be necessary in order to effect a cure. In pyometra due to an obstructive lesion in the cervix causing cervical stenosis the prognosis is usually poor or hopeless for the future breeding life of the mare. In urovagina, "urine pooling," the prognosis is guarded to poor.

A uterine biopsy and a knowledgeable prognosis based on the histopathological findings in conjunction with a complete clinical history and examination of the genital tract is very helpful in the prognosis of endometritis which may vary from mild to severe and be associated with other pathology including endometrial fibrosis, atrophy,

degeneration, hypoplasia or hyperplasia. The prognosis for recovery and future breeding success should be guarded in older barren mares with a history of abortion, pyometra, and infertility. The technique of uterine biopsy will be discussed later in this Chapter.

Treatment of genital infections in mares. The suturing of the upper part of the vulvar lips, the Caslick operation,⁷⁴ sexual rest, and possibly antibiotic intra-uterine infusions enable the veterinarian to give a much more favorable prognosis in cases of uterine infections than was possible previously.^{58,227,240} Early detection and treatment of genital infections of mares is essential to prevent sterility, early embryonic deaths, and abortions.

Most genital infections in mares can be prevented by proper hygienic handling of the mare and stallion at the time of breeding, by proper attention and hygiene applied to the mare at foaling, by close observation, culturing, and proper sanitary procedures in examining and treating mares, if necessary, prior to breeding. The control of genital infections causing sterility or infertility in mares is mainly a matter of preventative therapy and hygiene. This point cannot be stressed too strongly.

The vulva-suturing or Caslick operation, to prevent pneumovagina or the sucking of air and debris into the genital tract has been well-described^{239,301} and is performed as follows: the tail is bandaged and the perineal region and vulva carefully cleansed with soap and water. The mare is restrained by means of a twitch being placed on the nose and one foreleg being picked up. If the mare is excitable or vicious, a tranquilizer such as zylazine HCL or promazine HCL may be given intravenously for sedation. The mucous membrane of the vulvar lips is anesthetized by infiltration with a local anesthetic solution such as procaine, lidocaine or carbocaine, from 1 inch (2 cm.) below the level of the floor of the pelvis or ischial arch to and including the dorsal commissure, to a depth of .5 inch (1 cm.) from edges of the lips of the vulva at the mucocutaneous junction. In the hypersensitive mare it is desirable to anesthetize a small area of the mucous membrane at the border of the vulvar skin by holding a pledget of cotton that has been soaked in lidocaine or a similar anesthetic that can be applied locally before the 22 to 23 gauge needle is inserted. The mucous membrane elevated by the local anesthetic solution is removed by scissors after stretching each vulvar lip with forceps applied at the dorsal commissure. The scarified edges of the vulvar lips are brought together by separate nylon sutures placed about one-fourth to three-eighths inch apart or by a continuous interlocking suture. An oily antibiotic may be applied to the suture line to prevent dry scabs and make removal easier. The sutures are not tightened too firmly inasmuch as they may cut

the tender tissues. Union takes place rapidly and the sutures can be removed about the tenth day after the operation. The administration of tetanus antitoxin is probably not necessary but in valuable mares not protected by tetanus toxoid, it may be a justified precaution. This operation effectively prevents pneumovagina in most barren, infected mares and should be used on any mare if this condition is present or suspected. In mares in which pneumovagina is well-established, the vulva must be kept carefully sutured for the rest of the mare's breeding life since once this operation becomes necessary, seldom does the mare return to normal. An exception to this is the occasional young maiden mare that was sutured at the track that can be "opened" at the breeding farm and doesn't require further suturing. If the vulvar opening is too small, the adhesion between the vulvar lips should be incised after injecting the area with a local anesthetic solution to make the vulvar opening large enough to admit the penis at breeding. A stay or protective suture is usually inserted at the dorsal portion of the incised vulvar lips to prevent tearing or trauma to the vulva or intact previously sutured area at the time of coitus. If the mare is to be bred again in 2 to 3 days, this stay suture may be allowed to remain in place. The stay suture is usually made of a double thickness of one-fourth- or one-eighth-inch umbilical tape or heavy linen thread inserted into the anesthetized vulvar lips one-half to three-quarter inch, 1 to 2 cm. from the edges and tied rather tightly. A breeding or stallion roll should be used at the time of all natural covers on sutured mares.²⁴⁰⁻²⁴³ Following service in cases in which incision of the vulva was necessary, it should immediately be resutured. At the time of parturition, or 7 to 14 days beforehand, if a veterinarian is not to be present at the time of the mare foals, the vulva is opened by a blunt-pointed bistoury or sharp scissors after local anesthesia has been administered. After foaling the vulva should be resutured promptly. In the mare the vulva-suturing operation is the single most important procedure in the treatment of pneumovagina and sterility due to infection of the genital tract. Once it is indicated and undertaken it usually must be continued for the breeding life of the mare. As mentioned previously the easy and successful performance of the Caslick operation to greatly improve fertility in many Thoroughbred mares may be perpetuating and increasing the number of mares with poor perineal conformation that require this operation.¹⁸²

The vulva of normal mares may be temporarily sutured or clamped after foaling, especially if vulvar lacerations or a retained placenta occur, to prevent pneumovagina until the genital tract returns to normal in 1 to 2 weeks. In a few mares windsucking may occur only

during estrum or after service when the vulva is relaxed. These mares benefit from temporary closure of the vulva until the vulvar tone returns. When the vulva is temporarily sutured or clamped, scarification is not performed. The vulvar lips are simply pulled firmly together, usually by means of nylon sutures.

Following the Caslick operation most mares overcome the infection of the genital tract within 1 to 6 months, depending on the severity of the infection, without further treatment, since reinfection due to sucking of air and debris into the vagina is not recurring. These mares should not be bred until the infection is overcome. This emphasizes the necessity of checking and treating barren, infected mares during the fall season or a number of months before the breeding season. Although some mares with mild streptococcal infections may conceive, early or late abortion may result, or the foal may be diseased at birth, or the placenta retained at the time of parturition. The use of antibiotics parenterally and locally as intrauterine and intravaginal infusions or douches in the genital tract may precede closure of the vulva and result in a greater number of cures in a shorter length of time. The Caslick operation alone, together with a proper period of sexual rest, results in a high rate of recovery.⁸⁴ Of 36 infected mares on which this operation was performed because of vaginitis and cervicitis and evidence of pneumovagina, 22 or 61 percent became pregnant the next season. No other treatment was used.

In rare cases of pneumovagina associated with a horizontal vulva and a sunken anus in which the Caslick operation does not correct the pneumovagina or urovagina (urine-pooling), more extensive perineal surgery is indicated. This may require removal of skin in the lateral and caudal areas of the perineal region to draw the anus caudally, separation of the anus and vestibule to permit the vulva to assume a normal horizontal position, urethral extension or other procedures or combinations of "plastic" surgery to permit possible conception. In these severe cases the prognosis should be guarded to poor for future fertility.

The value of sexual rest following the Caslick operation, to allow the natural body defenses to overcome infection, is well proven. It has been observed frequently that apparently normal mares infected on the ninth day or foal estrus, if not bred, will in many cases free themselves of infection by the second estrum, about 25 to 30 days after parturition. Breeding on foal estrus, should not be practiced: if the placenta weighs over 14 pounds; if the foal is weak, deformed, or dead at birth or dies soon after birth; if the mare needs assistance in foaling; if the mare has abnormal discharges either in color, quantity, or consistency during the first week after par-

parturition; or if the genital tract is not free from any sign of infection, inflammation, or trauma when examined¹⁵² and possibly cultured on the seventh or eighth day after foaling. In some mares even longer periods of sexual rest are required. If a mare foals late in the breeding season and is infected, it may be desirable to hold her over until the next breeding season for service. In mares having difficulties such as retained placenta, dystocia, or severe infection and metritis at or after parturition, treatment and sexual rest for 2 to 3 months or until the following year may be indicated. As discussed previously mares may be treated locally and systemically by antibiotics on foal estrus if parturition was abnormal. Some mildly affected mares may be treated with PGF_{2α}, 10 mg, 7 days after foal heat and bred on the second induced cycle about a week sooner than if a prostaglandin had not been administered.

Some mares suffering from one or more of these conditions at parturition or after an abortion have a metritis and a delayed involution of the uterus. This can be determined by the breeding history, by the presence of a chronic uterine infection and discharge, and by a rectal examination that reveals a large, thick-walled uterus possibly containing varying amounts of mucopurulent exudate. Frequent douching of the genital tract of the mare at estrus with a mild antiseptic solution, such as weak **Betadine**, or **Novalsan** (chlorhexidine) solution, may assist in correcting mild inflammatory conditions. Too irritating solutions should be avoided as they may cause prolonged endometrial inflammation, ulceration, and possibly adhesions in the uterus and cervix.^{37,184} A 10% (3 ml. in 30 ml. of saline) Lugol's solution was irritating to the endometrium. A plastic indwelling uterine infusing instrument was developed^{165,239} permitting frequent infusions of the uterus with antibiotics or antiseptics. The value of such a catheter is limited and questionable. The author has experienced difficulty in having mares retain the instrument. Nevertheless douching under sanitary procedures at intervals of 1 to 2 days during estrus with a very mild chlorine solution, 50 ppm, a warm physiological saline solution alone, or physiological saline solution to which some penicillin, streptomycin, or broad-range antibiotic, such as a tetracycline, nitrofurazone or furacin, polymyxin B and/or neomycin combinations, have been added, may aid in hastening involution of the uterus and correction of the metritis and vaginitis. If the type of organism(s) causing the infection is known and the sensitivity of these organisms to the various antibiotics has been determined, select the antibiotic that will be most effective. These solutions may be pumped into or run into the uterus by gravity. If a mucopurulent exudate is present in the uterus,

this should be removed by douching and siphoning from the genital tract. Some veterinarians use antibiotics infused or inserted in an oil or tablet form into the uterus and left there to hasten recovery. Stilbestrol or estradiol in 20- to 30-mg. doses intramuscularly may be useful. In some of these cases the Caslick operation may be necessary. Exercise in moderate amounts may have value in improving the tone and hastening the involution of the uterus after foaling.

In recent years the use of antibiotics for uterine infections in mares has become widely practiced.^{239,243} With the large number of antibiotics and combinations of sulfonamides and estrogens available, each veterinarian treating genital infections of mares uses his favorite intrauterine preparations or combinations. In general, penicillin, nitrofurazone and the broad-range antibiotics such as terramycin or oxytetracycline, aureomycin or chlorotetracycline, tetracycline and ampicillin are most effective against streptococci and the Gram-positive organisms. Streptomycin, neomycin, chloramphenicol, polymyxin B sulphate, gentamicin¹⁹⁹ and amikacin sulfate⁵⁵ are most effective against *E. coli*, *Ps. aeruginosa*, *Klebsiella pneumoniae* and other gram-negative organisms.^{78,278} Some veterinarians put these products into oil or into saline.^{227,239} Amounts of 50 to 250 ml. are usually used for instillation into the uterine lumen. Most veterinarians prefer to treat the uterus 2 to 5 times at 24 to 48 hour intervals during estrus when the natural uterine defense mechanisms are active. Clitoridectomy and or sinusectomy as in the therapy for CEM may be necessary in persistent *Klebsiella* infections in mares.

Because of official regulatory requirements for the treatment of this reportable disease of CEM, therapy is given separately from other genital infections of mares. **H. equigenitalis** is sensitive to a wide range of antibiotics and antiseptics including penicillin, ampicillin, neomycin, chloramphenicol, gentamicin, tetracyclines, nitrofurazone and chlorhexidine. The latter two drugs are used most commonly in the local treatment of the genital organs of infected mares and stallions with a high percentage of cures when properly applied.

Presently it is necessary to perform a clitoral sinusectomy on suspected or infected mares before antimicrobial treatment of the genital tract. Because of the small openings of the sinuses, swabbing for culture and treatment is difficult or impossible.⁸ After sedation, often with zylazine (**Rompun**) and restraint, 20 to 50 ml. of lidocaine or carbocaine is infiltrated in the region around and under the clitoris. Stay sutures are placed in the lower vulva and clitoris to assist in the careful surgical removal of the entire sinuses (sinusectomy) and fossa or the complete removal of the sinuses, clitoris and fossa (sinusec-

tomy and clitoridectomy). The use of a small probe to delineate the depth and location of each sinus is essential to its complete removal. After either type of operation the wound produced may be left open to heal or sutured to more completely obliterate the clitoral fossa.^{106,161} This operation could be performed on the pregnant mare but in most cases it is deferred until after foaling. Excised sinuses of possibly infected mares should be sent promptly under refrigeration to an approved laboratory for culture. Although swabbing, culturing and treatment of quarantined mares and stallions, along with adequate records has resulted in the apparent eradication of the disease (CEM) in the U.S., the use of artificial insemination of mares with CEM-free semen or semen from an infected stallion to which antibiotics have been added, particularly gentamicin^{23c} may be of value in the future under certain extenuating circumstances.

Treatment of infected or suspect stallions or mares require their isolation and quarantine until the treatment and subsequent repeated swabbings and cultures are completed.^{8,109,159} These animals should have their external genitals cleansed thoroughly with warm clean water. This should be followed by a thorough cleansing and "surgical" scrub with a 2 percent chlorhexidine in a detergent base (**Novalsan Surgical Scrub**, Ft. Dodge Laboratories) of the erect penis, prepuce, and urethral sinus of the stallion and the external genitalia, vulva, vestibule and clitoral area of the mare. This is followed by a wash of clean warm water and drying. Then 0.2 to 0.3 percent nitrofurazone ointment (**Furacin Ointment**, Eaton Laboratories) is carefully applied in and to the above areas. This treatment is repeated at daily intervals for 5 treatments. After a rest of 7 days, swabbing and culturing in the aforementioned manner is then carried out. The uterus, cervix and vagina may also be infused daily for 5 days with 50 ml. of a lower concentration, 0.05 to 0.25 percent of a chlorhexidine gluconate solution, as higher levels are irritating. Most open mares spontaneously eliminate the infection from the deeper areas of the genital tract, vagina, cervix, uterus and uterine tubes after a few weeks or months. Parenteral and local antibiotic treatment of mares for CEM has not proven to be necessary or highly effective. Acute cases of CEM may not require treatment as the mare's natural defense mechanisms rather rapidly eliminate the organism from the uterus of the cycling mare.^{63,66}

Since CEM is a highly contagious venereal disease, spread of the disease in the breeding shed is highly possible as it was with vibriosis in bull studs.^{234,300} Strict aseptic carefully supervised procedures in the breeding shed are essential including the use of disposable plastic gloves and plastic pail liners, careful breeding hygiene

before, during and after service or semen collection, and the use of sterile individual equipment and material for cleaning the genitals, examination and insemination. Veterinarians supervising breeding shed hygiene should eliminate all possible avenues of genital contamination or spread of organisms between all animals except the two animals being bred. This requires establishing a rigid step by step procedure, training and acceptance of these procedures by the attendants in the breeding shed and the continued monitoring of these procedures by the veterinarian. Such a practice could also control infections other than CEM.

If present control and eradication measures are not adequate or are ineffective, artificial insemination and the development of a vaccine might be developed to minimize or control the infertility associated with CEM. Vaccination of ponies against CEM with a killed bacterin from *H. equigenitalis* provided a degree of immunity but did not protect them from developing the disease when challenged.^{107b}

CEM is a reportable disease and any suspected outbreaks with signs of a genital discharge soon after service, short estrous cycles and infertility should be reported to the state and federal regulatory officials as well as to owners of mares and stallions possibly exposed to the infection. Because of the great mobility of equine racing, breeding and show animals within and between countries and states, most animal regulatory agencies in each country have formulated and put into law regulations, codes or requirements pertaining to the importation and movement of horses to control or prevent the spread of CEM.^{1,6,10} and other diseases. These codes or regulations require strict adherence to testing, identification, treatment and quarantine procedures. These codes or regulations are promulgated yearly and changes in them are made as further information on CEM and its epidemiology are developed.

Most cultures positive for molds or fungi and yeasts, *Aspergillus*, *Mucor* and others and *Candida*, are a result of contamination of the upper genital tract and they do not cause severe inflammatory reactions with endometritis and are rapidly eliminated spontaneously.⁴⁸ Occasionally they do produce a severe inflammation with invasion of the endometrium and a well-established infection as determined by biopsy. This may occur after intensive prolonged antibiotic therapy for a bacterial infection resulting in the introduction of the opportunistic fungi or yeast into the uterus, especially in infection-prone mares. Fungi are common in the environment of mares and frequently contaminate culture swabs, plates or media and provide erroneous readings. Although weak iodine solutions, Lugol's and Betadine, and systemic io-

did therapy have been used in the past for treatment, presently nystatin, 500,000 I.U. daily for 5 days, amphotericin B²³¹ and clotrimazole 400 to 600 mg. uterine infusions every third day for 3 to 4 treatments have been recommended. This latter drug, a human product, is available in suppository form which may be inserted into the mare's uterus.¹⁴⁴

Antibiotics given parenterally are of little value in chronic uterine infections.²⁴¹ Local treatment is indicated. Systemic treatment is indicated in acute or severe uterine infections causing a pyemia or septicemia as may occur after parturition. Autogenous bacterins have been used with some success in genital tracts infected with *Klebsiella* or *Pseudomonas* organisms in mares.^{26,58,59} Further controlled studies on the value of autogenous bacterins against specific infectious organisms are needed since spontaneous recoveries in mares after a period of several months or more of sexual rest are not uncommon. If the Caslick operation is indicated it should be performed, since antibiotic therapy alone cannot permanently correct a genital infection due to pneumovagina. Genital rest will aid recovery, and bacteriological and cytological or histopathological examinations of the uterus will indicate when breeding can be undertaken with an expectancy of conception.

In mares with pyometra not due to an obstructed or sclerosed cervix, that are anestrus due to a persistent CL with an elevated, >2 ng/ml, plasma progesterone level should be treated with a luteolytic dose of prostaglandin or prostaglandin analogue²⁵ to evacuate the uterus and followed by antibiotic therapy of the uterus during the induced estrous period.

Infections of the genital tract secondary to severe injuries to the perineum or from recto-vaginal fistulas require the repair of the trauma-induced lesions in order for subsequent conception to occur. However, the author and others^{241,243} have observed rare cases of mares that have had a recto-vaginal fistula that conceived and delivered a normal foal. Conception in mares with severe injuries involving the recto-vulvar area are not uncommon because of the protection provided the vagina by the vestibular-vaginal sphincter and folds of mucous membrane in that area that prevent pneumovagina.

Barren older mares with a history of recurrent chronic endometritis even though they were free of infection in their genital tract at the time of service or experimental exposure to infectious bacteria such as streptococci or *Pseudomonas* organisms, showed a greatly reduced uterine and cervical reaction with an increase in polymorphonuclear leucocytes as well as eosinophiles in the endometrium. These older susceptible, infection-prone mares exhibited less mucopurulent exudation and a persistence

of the infection and developed a chronic endometritis. There was definite evidence that these chronically infected mares or those that readily become infected had a breakdown or alteration in the non-cellular defense or bactericidal mechanisms in the uterus which set them apart from the normal, healthy, often young mares which exhibit an excellent, prompt, highly effective defense mechanism. There apparently is a delicate balance between the pathogenicity of the infective bacteria and the susceptibility of the mare to infection.^{134,135,137,220} Infection-prone, often older, mares are highly susceptible to uterine infections or endometritis after foaling and after each service period unless preventive therapeutic procedures are taken.

Twelve to 24 hour postbreeding or postovulation antibiotic treatment of the uterus using 250 to 500 ml of an antibiotic solution reduced the uterine bacteria present from the natural service or present in the uterus at the time of service and prevented the infection from becoming established in many susceptible mares.^{163,275} This greater susceptibility to infection and infertility after service in older pluriparous mares that often had a local dilation of the ventral portion of the base of the uterine horns or in the body of the uterus was noted.¹⁶³ In these locally dilated areas the mucosal folds were flattened and the endometrium was atrophic and aglandular. The rest of the uterus was normal. In a subsequent large study employing post-breeding antibiotic uterine treatment of mares no benefit was demonstrated by such therapy.³⁰⁴

A review of the antibacterial drugs used in the uterus of the mare concluded that this therapy is of secondary importance to good management and breeding hygiene. But in individual mares following proper diagnostic procedures, antibiotic therapy along with induced estrus, using the prostaglandins, and sexual rest could be useful in restoring fertility in certain mares.⁸⁶

Many stallions may harbor *Pseudomonas*, as well as *Streptococcus zooepidemicus*, *Klebsiella* and other bacteria, fungi and yeasts.^{26,27,134,137,257} Elimination of these infections from stallions is very difficult and usually unsuccessful. Most of these infectious organisms in stallions are not highly pathogenic, but a few stallions may apparently carry and transmit virulent organisms that infect a large number of mares bred to him. This fact further accentuates the necessity of careful hygiene in the breeding act. As noted previously excessive use of antiseptics on the stallion's genital organs such as Novalsan and Roccal, may cause the development of resistant gram-negative bacteria that cause more serious problems.^{51,202}

In breeds of horses where artificial insemination is practiced the control of the bacterial flora in the extended

semen with antibiotics is indicated especially for the infection-prone mare where the infection has been eliminated, but coitus would probably reestablish the endometritis.^{135,239,289} These authors recommended adding 1000 units of potassium penicillin, 1 mg. of dihydrostreptomycin and 200 units of polymyxin B. sulphate per ml. of skim-milk or cream-gelatin diluter (see Artificial Insemination in horses) and inseminate with semen extended 1:1 or 1:4. The latter report²⁸⁹ recommended that 1000 units of polymyxin B per ml. be added to fresh skim-milk extender to control both *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. The warm semen should be added to this warm semen extender containing antibiotics and incubated at body temperature, 38° C, for 15 to 30 minutes before it is used to inseminate mares. In breeds permitting the registry of foals conceived by artificial insemination, the use of this practice with semen extender with antibiotics, along with strict management and hygienic practices, has resulted in improved, 10 to 20 percent, foaling rates versus natural service and less supervised management.⁹⁹

Thus for infertile, infection-prone, usually older, mares who often have a moderate degree of endometrial fibrosis and infiltrative endometritis as determined by endometrial biopsy, careful breeding management and hygiene at the time of service is imperative. Limiting the number of services in an estrous period to one or possibly two and/or the use of HCG to shorten the estrous period and hasten ovulation is desirable. The use of the post-service uterine infusions of antibiotic solutions and the use of artificial insemination with extenders containing antibiotics have been practices that have been proven to be of value in improving the foaling rate of these infertile mares.

Because each of these above procedures or practices have shown merit, Kenney and Rosedale and Ricketts have developed and modified them into minimal contamination techniques (MCT) for breeding mares.^{156,239} The former study¹⁵⁶ reported that even when the penis and sheath of stallions were carefully washed with soap and water and rinsed before service, the ejaculate from most stallions contained 4 to 36 million colony-forming units (CFU) of a variety of Gram-positive and negative bacteria. Thus this semen could readily reinfect the susceptible uterus. The following minimal contamination techniques were designed for breeds which permit artificial insemination and those mandating natural service.

A. Minimal contamination technique for artificial breeding:

1. The stallion is trained to mount a phantom located in a clean, dust-free area and ejaculate into a clean, sterile artificial vagina. The latter

is sterilized by washing in hot water and non-residue soap, rinsed thoroughly with hot water and disinfected in 70% ethanol for several hours. Before use the artificial vagina (AV) is rinsed in hot water and physiological saline solution. A thin film of a non-spermicidal lubricant such as KY jelly is spread through the AV with the arm covered by a plastic sleeve.

2. The stallion, before semen collection, is sexually aroused and the penis and sheath are carefully washed with a warm soapy non-detergent water which is removed by multiple warm water rinses. (If a quiet mare is used for a mount instead of a phantom her tail should be bandaged and her buttocks and perineal region carefully washed and rinsed. Before permitting the stallion's penis to enter the AV the penis of the mounted stallion should be drawn to the side to allow the discharge of some of the urethral gland or preperm fraction to flush and remove bacteria from the urethra.
3. After collection of the ejaculate in the AV, it is poured through a sterile in-line milk filter into a sterile warmed beaker to remove the gel fraction. The semen is evaluated for motility, number of normal spermatozoa and pH.
4. The ejaculate is "washed" by adding equal parts of a warm extender containing antibiotics followed by centrifugation at 1500 rpm at 300 Gs for 3 minutes. The supernatant is removed and the spermatozoa are suspended in warm extender and drawn into a sterile syringe and capped. Depending on the fertility of the stallion 200 to 500 million motile normal spermatozoa are used for each insemination. This warm syringe after being wrapped in paper towels for insulation is placed in a bag and put at refrigerator temperature, 4° C, for at least one hour before insemination to permit the antibiotics to eliminate any bacteria that might be present.
5. The mare to be bred is then inseminated after wrapping her tail, and thoroughly scrubbing and rinsing her perineal and vulvar region with Betadine or Novalsan scrub followed by 3 warm water rinses. The inseminator uses a sterile plastic sleeve over which he places a sterile disposable rubber glove. The back of the hand is lubricated with KY jelly and with the tip of the inseminating pipette covered by the index finger, the vulvar lips are parted and the hand and arm are inserted into the vagina. The index finger guides the pipette into the cervix and then

the pipette is pushed a few inches further cranially and the extended semen is infused into the body of the uterus.

B. Minimal Contamination Technique for Natural Service:^{156,239}

1. Both the mare and stallion are prepared as described in A above but just before service the uterus of the mare is filled, so that slight overflowing into the vagina occurs, with 100 to 300 ml. of warm semen extender containing antibiotics. Care should be taken so that ballooning of the vagina, pneumovagina, does not occur before service that follows immediately after the introduction of the extender. Thus the stallion ejaculates directly into this antibiotic containing extender.

Satisfactory results have been reported for the use of this technique. Usually only one service per estrous period is desired so careful estimation of the time of ovulation or the use of HCG are indicated. These infection-prone, infertile mares in which the above MCT technique is employed should be cycling regularly and bred during the most fertile portion of the breeding season.

A simple easily prepared semen extender has been described^{156,239} consisting of:

Instant, non-fat or low-fat skimmed milk—	2.5 gms
Glucose—	5.0 gms
(Gelatin BP) (optional)—	(0.5 gms)
Sterile distilled water—	100 ml.

Antibiotics added to this extender may be either—

300 mg or 150,000 units of crystalline penicillin and
 300 mg or 150,000 micrograms of crystalline streptomycin or
 100 mg of gentamicin sulphate

Other extenders with antibiotics at levels that don't effect spermatozoan activity or fertility have been described.²⁵⁹ (See Chapter on Artificial Insemination.) Several authors^{99,156,239} have indicated that careful breeding management and hygiene, service to highly fertile stallions and a minimum contamination technique either by AI or natural service should be used on the infertile, infection-prone, often older, mares in Categories II and III as defined by endometrial biopsies, breeding history and clinical examination. If obvious clinical endometritis is present, correction of the pathological condition is necessary before breeding can be recommended. This therapy may require several months or more.

Endometrial Biopsy

Although earlier studies reported on endometrial biopsy techniques^{121,164,282} the technique for collection of a suitable sized biopsy and the variety of histopathological findings and their relation to fertility in mare were first adequately reported by Kenney¹⁵⁴ and since corroborated by others.^{92,99,154,239,251} Presently endometrial biopsies are used widely as an aid in evaluating the degree of fertility in mares, particularly those barren mares without clinical lesions or infections of the genital tract.^{92,154}

The procurement and processing of an endometrial biopsy specimen should be preceded by a careful physical examination of the genital tract, obtaining a detailed breeding history and a careful collection of a swab specimen of the uterine lumen for the detection of bacteria that has been described. The specimen is obtained by means of a sterile alligator-jawed (rounded) biopsy forceps 55 to 70 cm. in length with a basket 20 by 4 by 3 mm. in size. The mare should be restrained for a rectal examination. The tail should be bandaged and the feces removed from the rectum. The perineal area and vulva should be washed with soap and water and rinsed 3 times with water. The arm should be covered with a plastic sleeve and this is in turn covered by a sterile rubber glove lubricated with sterile lubricating jelly without disinfectants. The vulvar lips are parted and the hand cupping the punch or forcep is inserted into the anterior vagina. The biopsy forcep is guided through the cervix with the index finger. After the forcep has entered the uterine body the hand is removed from the vagina and inserted into the rectum where it guides the forcep to the area of the bifurcation of the horns, near the implantation site. The jaws of the forceps are opened and uterine wall and endometrium are gently pushed laterally into the jaws by the rectal hand and the jaws are shut tightly. The biopsy forcep is withdrawn from the genital tract. Care should be taken to avoid penetrating the uterine wall with the forcep, as might occur if a straight cranial bite is made.

Usually the biopsy specimen is taken from the cranial dorsal portion of the uterine lumen. A single biopsy specimen has been shown to be representative of the entire uterine endometrium.³⁹ However if any abnormality of the mare's uterus is noted a biopsy specimen from that area or from several areas may be obtained. The biopsy specimen may be taken at any stage of the estrous cycle and even within a few hours after breeding. However if the mare has been bred and ovulated, taking the uterine biopsy a number of days later, as discussed previously may result in luteolysis or regression of the CL and the induction of estrus with a shortened estrous cycle. If biopsy specimens are taken at the end of the breeding

season from barren mares a mid-diestrous sample was recommended.²³⁹

The suitable-sized endometrial specimen is removed from the forceps with a hypodermic needle and placed preferably in Bouin's fluid instead of 10% formalin. After 2 to 24 hours the specimen is placed in 70% ethanol or 10% formalin and sent to the laboratory for skilled histopathological examination. The prognostic or diagnostic value of a satisfactory endometrial biopsy specimen in predicting the fertility of a mare not only requires an evaluation of the breeding history and a careful complete clinical examination of the mare with appropriate laboratory tests but also the examination of the biopsy specimen by an individual who has experience and training to interpret the lesions observed.

These endometrial lesions have been reviewed and categorized.^{92,99,154,155,239} They include varying degrees and combinations of histopathological conditions of: (a) **periglandular fibrosis**, either focal or widespread, often associated with cystic distention of the uterine glands, slight to severe, (b) **inflammation or endometritis** which may be acute, chronic, infiltrative degenerative, widespread or focal, (c) **lymphatic stasis** with lacunae, (d) hypertrophy and hyperplasia, focal or diffuse, (e) atrophy and hypoplasia, focal or diffuse.

The many variable lesions observed in these histologic sections, especially during various stages of the estrous cycle, require skilled experienced observers to assess their significance. Atrophy of the endometrium is commonly associated with seasonal anestrus and inactive ovaries. Hypoplasia is noted in postpuberal fillies and mares with congenital or chromosomal abnormalities.^{49,57} Inflammation if mild or moderate may not be associated with uterine infections. The stage of the estrous cycle also importantly influences the findings observed. It is possible that degeneration of the endometrium and infertility as discussed earlier in cattle associated with delaying service until heifers were 4 or 5 years of age (DeLange) and in unspayed nulliparous dogs (Dow and others) may be implicated in the decline in fertility in nulliparous mares of middle or older age and be an important factor in susceptibility to endometritis in older mares as it has in older dogs. Most pathologists and others^{92,99,251} trained and ex-

perienced in noting the endometrial histologic or pathologic changes have followed the general three categories outlined by Kenney.¹⁵⁴ However Ricketts^{233,239} has listed 14 histopathological groups of various combinations of lesions for predicting the fecundity of mares.

The three categories outlined by the former¹⁵⁴ are:

Category I—the endometrium is essentially normal with no pathologic changes or if a few are present they are slight and widely scattered,

Category II—frequent scattered mild to moderate fibrotic changes and light to moderate diffuse infiltrations or scattered but numerous foci of inflammatory changes. Widespread lymphatic lacunae or atrophy of the endometrium may be present,

Category III—widespread severe periglandular fibrosis of the endometrium and widespread severe inflammatory changes with moderate to heavy infiltration of plasmacytes. Lymphatic lacunae are extensive causing the uterine wall to be edematous or flabby- or jelly-like on palpation. Endometrial hypoplasia due to chromosomal anomalies and severe chronic pyometra should also place mares in this category.

Ricketts²³⁸ has shown the poorest post-biopsy breeding performance of mares is associated with endometrial atrophy not associated with winter anestrus, chronic infiltrative endometritis, chronic degenerative endometritis and endometrial hyperplasia and especially combinations of these pathologic changes.

Categorizing mares based on endometrial biopsies together with clinical examination of the genital tract, the mare's age, and the breeding history, number of years barren, has been shown by a number of studies^{92,99,154,239} to be of value in estimating and predicting the future fecundity of mares.

Although the time of and diagnostic methods for determining pregnancy or conception and the time interval from biopsy to the termination of the study varied, pregnancy loss from mare categories I, II and III were 10, 24 and 44 percent, respectively.^{92,251} This indicated that endometrial disease is probably an important cause of embryonic or early fetal death. Further, more continuing and refined studies should be conducted. In 92 clinically normal infertile mares only 30.4% (28 mares) were pos-

Foaling Rates Based on Endometrial Biopsy

Kenny (244 Mares) ¹⁵⁴		de la Concha-Bermajillo and Kennedy (79 Mares) ⁹²	Doig et al. ¹ (403 Mares) ⁹⁹	Shideler et al. (332 Mares) ²⁵¹
Category I	68%	78%	82%	61%
II	51%	55%	74%	48%
III	11%	36%	46%	35%

¹Of 4 categories listed the last was omitted as 8 mares none foaled.

itive on culture and only 18% of the 28 mares, had evidence of endometritis on biopsy examination.⁹⁹ Furthermore in this study 75 percent of the mares had varying degrees of endometrial fibrosis and although exceptions occurred generally older mares were in the lower categories. Thus endometrial biopsy is only one of the aids in predicting the fertility of a mare.¹⁵⁵ No mare should be classified as incurably sterile except in exceptional, severe, advanced and obvious pathologic conditions that would prevent conception or a normal termination of pregnancy.

Other Infectious Diseases of the Genital Organs of Mares

Coital vesicular exanthema, genital horse pox or equine venereal vulvitis or balanitis, is a viral disease of horses reported worldwide. The causative agent is equine herpesvirus 3 (EHV3).^{45,62,216,217,267} This virus does not cause abortion. It may cause a mild nonclinical upper respiratory infection if inoculated intranasally. The disease is rather uncommon in the United States. It is generally believed to be transmitted by coitus but the virus apparently may be readily transmitted by other means as it spreads very rapidly through a band of mares. In rare cases even young foals may be affected.^{287,305} The incubation period is short, 2 to 10 days. No fever, anorexia, or other signs of a systemic reaction are present. The disease appears suddenly, and often the source of infection is unknown. The disease is characterized by the early appearance of many papules, vesicles and pustular scabby erosions 1 to 3 mm in diameter that may become confluent of the skin of the vulva, penis and prepuce.^{62,216,217} These lesions exude serum that dries and forms crusts. (See Figure 147.) When these crusts are rubbed off, a punched-out, irregular ulcer or erosion 0.5 to 1.0 cm. in diameter is observed. These erosions enlarge and coalesce and become filled with exudate and dried scabs. The duration of the acute disease is about two weeks. Intracellular inclusion bodies may be seen in the cells obtained from scraping the vulvar or preputial lesions. Lesions on the skin of the vulva heal leaving small nonpigmented spots. Antibodies to EHV3 are found in the blood serum. Occasionally lesions may be noted on the nose, lips and conjunctiva as well as the vulvar and vaginal mucosa resulting in a purulent discharge.^{216,267} The duration of the persistence of this virus is not known. In stallions coital exanthema develops on the penis, glans and prepuce. Some stallions may be reluctant or refuse to cover a mare due to pain until the lesions heal. Occasionally a secondary bacterial infection may occur. Some veterinarians will use mild astrin-



Figure 147. Coital Vesicular Exanthema or Genital Horse Pox in a Mare. (This is due to a herpes virus.) (Courtesy T. Clark, Iowa State Univ.)

gent protective preparations such as calamine lotion or other similar products on the lesions. Healing is usually rather rapid within 10 to 14 days even without treatment. Breeding activities should be suspended for 3 to 4 weeks or more until the infection has subsided and the lesions have healed. The disease does not affect fertility or cause abortion, but may cause a reduced libido in the stallion during the acute phase of the disease.²¹⁶ One attack does not confer permanent immunity. Affected animals should be quarantined for 60 days.

Dourine is a disease of horses due to *Trypanosoma equiperdum*, and is transmitted almost entirely by coitus. This was the only trypanosome disease of importance in domestic animals in the United States. Dourine is widespread throughout the world in temperate as well as tropical countries. It was first recognized in the United States in 1885 by W. L. Williams in Illinois, where it was believed to have been spread by a Percheron stallion imported from France. By the use of the complement fixation test and the destruction of all reacting animals, the disease was apparently eradicated from the states west of the Mississippi to which it had spread. In 1939 and 1940 another outbreak occurred in Nevada, California, Colorado, Arizona, New Mexico and apparently Mexico, affecting mainly the wild horses and horses of Indians living in rather isolated areas. Vigorous efforts at eradication were again undertaken and it is believed at

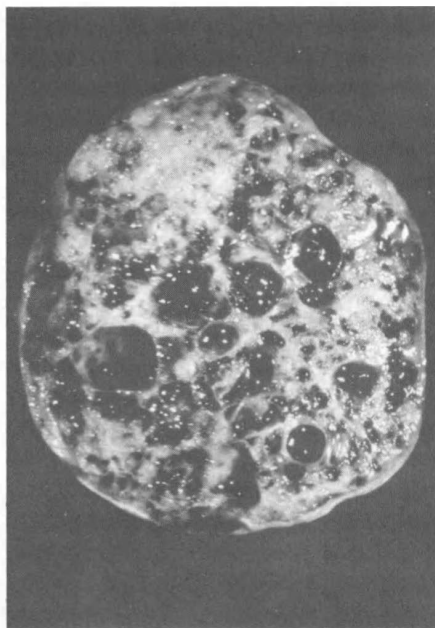


Figure 148. Granulosa Cell Tumor of the Mare's Ovary. (Note the hemorrhages interspersed throughout the tumor.) (Courtesy K. McEntee.)

present that dourine is probably eradicated from the United States.^{24,45}

Dourine is transmitted at coitus as a venereal disease. Members of the horse family are the only animals that contract the infection and therefore no other reservoirs of infection exist. Except in Europe the disease is chronic and the onset is slow. The incubation period is 1 to 8 weeks, or occasionally it may be much longer.⁴⁵ The disease may exist in the animal for months or years with the affected animal alternately improving and relapsing. In the terminal stages emaciation and nervous symptoms develop, rendering the animal worthless and it is usually destroyed.

The early symptoms of the disease are characterized by swelling of the vulva and vagina of the mare with a mucous discharge containing trypanosomes. The affected stallion's penis, prepuce, and scrotum become swollen and reddened and paraphimosis may develop. The swelling may vary in size. There may be a mucopurulent urethral discharge. On palpation the swollen area is nearly free from heat and pain. In mares genital irritation caused by this organism is evidenced by frequent urination and tail switching. After the acute genital symptoms subside, peculiar raised plaques appear in the skin over the body. These are often called "dollar" plaques because of their similarity in size to a silver dollar, though some may be much larger. They appear suddenly and

disappear within a few hours or days and are replaced by others. These plaques are said to be pathognomonic of the disease. Occasionally abortion may occur.³⁰⁵ Depigmentation of the mucosa and skin of the vulva, penis, and prepuce may occur. There are irregular periods of fever in the late stages of the disease and symptoms of paralysis, involving the facial muscles, the limbs, and the penis gradually develop. Emaciation progresses until death occurs. Mortality is estimated at 50 to 75 percent. The course of the disease may be a few weeks to several years with recurrent attacks or it may remain subclinical. Infected animals are spreaders. Treatment is expensive and impractical as results are poor. This is a reportable disease in the U.S.

Miscellaneous Pathological Factors in Infertility of Mares

Tumors of the genital tract in mares are uncommon. On examination of over 2,000 mares only 6 true tumors

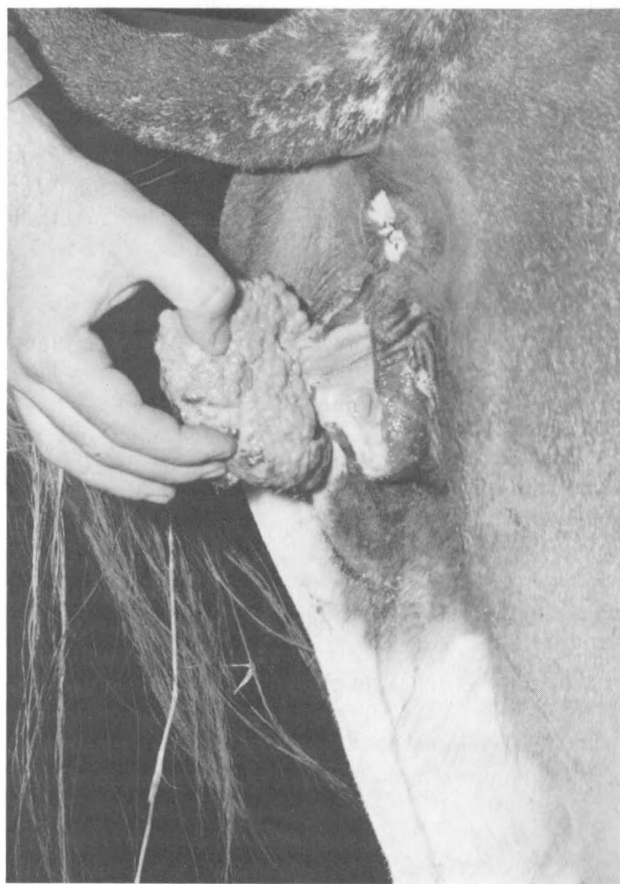


Figure 149 Squamous Cell Carcinoma of the Vulva of the Mare.

were reported.⁹⁷ Of these 6, 3 were in the ovary. Equine ovarian tumors, especially granulosa cell tumors are more common than tumors of the tubular genital tract.^{82,83,97,107,186,187,200,221}

Beta-cell adenoma in the pars intermedia of the pituitary gland in mares over 13 years of age causes a syndrome characterized by weight loss, muscle wasting, thin abdominal walls, poor, long hair coat that persists into the summer months with excess sweating, and often polydipsia, polyuria, hyperglycemia, glycosuria, posterior weakness or paresis, and elevated plasma levels of adrenocorticoids (Cushing's syndrome).^{94,104} These debilitated mares are usually anestrus. The condition becomes terminal within 6 to 18 months. Rarely adrenocortical tumors may produce similar signs.

Ovarian Tumors

The granulosa-theca cell tumor is the most common equine ovarian tumor. These tumors occur unilaterally and on palpation are greatly variable in size with a smooth, firm or lobulated surface with large fluid-filled cysts. On incision these granulosa cell tumors are yellow to white in color. Solid tissue and cysts along with areas of hemorrhage and necrosis are observed. Mares with reproductive failure, changes in sexual behavior or temperament and signs referable to abdominal discomfort should have their ovaries examined by rectal palpation. The granulosa-theca cell tumor should be differentiated from an ovarian hematoma that can reach a size of 20 or more cm. and persist for months. Mares with hematomas usually continue to cycle normally with no behavioral changes and the hematoma will regress in size while the tumor will gradually increase in size. Affected mares may have a history of anestrus or continuous estrus like a nymphomaniac mare. Others may exhibit stallion-like behavior of teasing or mounting mares along with squealing or roaring and the development of a heavy neck. Occasionally these animals may be hard to handle and aggressive toward other horses. Enlargement of the clitoris occurs in some cases. The ovary opposite from the affected ovary is usually small and inactive probably due to suppression of its activity by the steroid hormones from the tumor. As in cattle the mare may rarely become pregnant even with a granulosa cell tumor in its early stages of development when cycling is still regular.⁵⁰ All of the granulosa-theca cell tumors and probably related arrhenoblastomas^{194,263} produce hormones. Male-like behavior was associated with testosterone levels over 100 pg/ml that declined to about 20 pg/ml after removal of the granulosa cell tumor.²⁶³ Granulosa tumor cells do not

produce progesterone. Meagher et al. reported that 29 of 63 mares, nearly 50 percent, with ovarian neoplasms manifested male behavior. Anestrus behavior may also be due to high testosterone levels observed in 9 of 10 mares. Endocrine patterns in mares with granulosa cell tumors and exhibiting anestrus or estrus were similar although the latter had higher estradiol levels. Following removal of the affected ovary in 12 mares the unaffected ovary that was small and firm without any follicular growth returned to cyclic activity and ovulated a follicle 83 to 392, average 209, days later. Eight of the 12 mares did not show estrus until the next breeding season. One mare did not show cyclic activity following removal of the affected ovary before being killed 524 days later.²⁶³

The 78 mares with granulosa-theca cell tumors ranged from 2 to 20 years with an average age of 10 years.¹⁹² Mares that had foaled previously and maiden mares were equally affected. All tumors were unilateral with equal numbers affecting the left and right ovary. The tumor diameter ranged from 6 to 40 cm. with most in the 10 to 20 cm. range. Only 1 of the 78 granulosa-theca cell tumors metastasized; thus metastasis is much less common than in cows and humans. Only 6 of the 78 mares died from surgical complications. Normal behavior occurred postsurgically in most of the mares with regular estrous cycles developing in about 75 percent of the mares. Thirty, 77 percent, of 39 mares bred, conceived and produced live foals. The tumors may be surgically removed using the ventral midline, paramedian or flank approach.^{192,249} Great care is used to control hemorrhage and to invert the serosa over the ovarian stump to prevent adhesions.¹⁹²

Other uncommon equine ovarian tumors or cysts that have been reported are:^{50,82,83,97,111,125,175,186,187,192b,200,206,221,305}

Melanoma	Arrhenoblastoma ¹⁹⁴
Teratoma ^{50,111,186,192b}	Cystadenomas and cystodeno-
	carcinomas ^{50,83,107,125,187,200,206}
Lymphosarcoma ^{175,206}	Hemangioma ^{186,187}

Occasionally small masses or "rests" of adrenal cortical tissue are found in or near the equine ovary.^{157,187,210}

Germinal inclusion cysts or "fossa-cysts" are formed by peritoneal fragments that become imbedded in the ovary following ovulation. These "serosal" cysts may be large enough or numerous enough to be of clinical significance by possibly interfering with ovum transport in older mares.^{141,186,187,210} A case report described a 7 cm. ovarian cyst containing a bot, *G. intestinalis*.¹⁰⁰

Hematomas of the ovary are common.^{50,141,187,210} Hemorrhage into the ovarian follicle regularly occurs at ovulation and in anovulatory follicles.^{2,210} Hematomas

may vary in size from 5 to 20 or more cm. in diameter and persist for weeks or months. Normal cyclic activity usually continues in most cases.^{50,141} Depending on the age and stage of development of the hematoma repeated rectal examinations may reveal they are decreasing or increasing in size. The author observed a 20-year-old mare that bled to death from a follicle that ovulated during the third month of pregnancy. Histologic section did not reveal evidence of an early or small granulosa-theca cell tumor. These latter tumors may contain blood or rarely rupture and bleed intraabdominally. Varicosities of vessels in the equine ovary are common and may become large enough to palpate on rectal examination. Hemangiomas and hamartomas of the ovary have been described.^{187,232} Removal of large hematomas by unilateral ovariectomy has been described where an absence of normal ovarian tissue was observed.⁵⁰

Parovarian cysts are common in the mare and may vary in diameter from a few mm. to 5 to 6 cm. They are often found in the fimbria as small fimbrial cysts, hydatids of Morgagni, that usually cannot be palpated. The larger parovarian cysts originate from other remnants of the mesonephric or paramesonephric tubules or ducts and are located in the mesovarium near the ovary.^{187,210,234}

The epoophoron, a cystic remnant of the mesonephros is about 0.5 to 2.0 cm. in diameter and located in the ovarian capsule at the dorso-cranial-medial pole of the ovary. These cysts have no effect on the reproductive cycle or fertility. Large pedunculated parovarian cysts that caused strangulation of the rectum have been reported.³⁰⁵

Cases of ovarian hypoplasia and/or gonadal dysgenesis with chromosomal abnormalities associated with infertility, a phenotypic small to normal-sized mare, absence of an estrous cycle or only occasional estrus of a passive type, a small flaccid uterus, a flaccid cervix with an open os and small to very small ovaries, have been described with increasing frequency in recent years in many breeds of horses.^{64,49,57,133,141,143} The older reports of bilateral ovarian hypoplasia were probably associated with gonadal dysgenesis.^{210,234} Unilateral hypoplasia of the ovaries should be diagnosed with great caution, especially in nulliparous mares. Repeated examinations during the breeding season in these mares is indicated. As noted above small inactive ovaries are often associated with a granulosa-theca cell tumor in the opposite ovary.

The most common chromosomal abnormality found in 28 or 58%, of 48 mares¹³³ with gonadal dysgenesis was the 63,XO karyotype. This karyotype is similar to that found in women with Turner's syndrome but some phys-

ical differences exist. Affected mares have very small but palpable ovaries and a few germ cells may be in the ovaries.^{46,47,57} No sex chromatin or Barr bodies were found in these XO mares.^{46,49,57} Other chromosomal abnormalities included 63,XO/64XY, 64XY, 63XO/64XX and 64XO/64XY, 65XYY/64XX, 65XXY/64XX and 65XXX.^{46,57,141} Because of a lack of germ cells in the ovaries follicles usually don't develop and the ovaries are small, smooth and firm. It is likely that chromosomal abnormalities may be an important cause of infertility in mares. Cytogenetic studies are indicated in infertile mares showing some or all of the above signs. The relatively high incidence of mosaicism in sex chromosome anomalies of mares may reflect, as in women, that aging of the ovum and post-fertilization errors of mitosis may be fairly common in horses because of the long estrous period and variable time of service and ovulation.⁴⁶

Clinical effects of the XO anomaly in mares is limited to the abnormal development of the primary or secondary sex characteristics which may be difficult to recognize in mares.⁵⁷ Since mares with chromosomal abnormalities are nearly always sterile their detection by cytogenetic techniques would save considerable expense.

Lesions of the uterine tube in the mare are rare. As discussed previously, mild salpingitis associated with endometritis may be fairly common but obstruction of the uterine tube is rare. Infundibulitis with small fibrous adhesions in the fimbria around the ovulation fossa is common in the mare.²⁸⁸ Pyosalpinx has not been described in mares. Hydrosalpinx is also very rare although two cases; both unilateral, were described.⁹ The author is unaware of any reported genetic defects or arrests in development of the equine uterine tube. Rare cases of small under-developed fimbriae that might have difficulty in picking up ova have been reported.²¹⁰

Tumors of the Uterus, Cervix, Vagina and Vulva: Uterine tumors include **leiomyomas**, which are usually small and 1 to 2 inches in diameter or they may be multiple or rarely large, **fibromas**, **rhabdomyosarcomas**, and **carcinomas** which are rare.^{82,83,97,119,187,200,284} These tumors may also be found in the cervix and vagina. Squamous-cell carcinomas often in pintos, melanomas that frequently "metastasize" in white horses, and papillomas are the three most common tumors of the vulva of mares.^{82,83,107,200,221,266}

Other Pathological Changes in the Equine Uterus include:

Ventral uterine enlargements near the bifurcation of the body and uterine horns in older pluriparous mares have been described^{157,163} due to mucosal atrophy or focal myometrial atonia. The former probably follows the

latter and may be a natural consequence of the anatomy of the uterus and its supporting ligaments and the site of implantation and fetal development. Myometrial lymphatic lacunae or varicosities in this area may also contribute to this uterine enlargement.

Lymphangiectasis of the myometrium or lymphatic lacunae and possibly cystic endometrial hyperplasia^{153,157,187} with a flaccid, edematous, soft, thick, doughy or spongy uterine wall which in the opened uterus shivers like a gelatinous mass when jarred. Numerous submucosal cysts, 1 to 5 cm. in diameter under the glistening, moist mucosa may bulge into the uterine lumen. Advanced cases especially in older mares may have a mucometra with the uterine contents having a milky, gray to dark-brown color.^{9,11,157,187,277,310} If this condition is severe the mare is usually hopelessly sterile.^{97,227} Knudsen^{162,163} described 24 mares with lymph stasis of the endometrium in which lymphocytes predominated in the endometrial biopsy smears. Most of these mares had poor fertility; in 2 cases pregnancy terminated in early fetal death. These mares cycled normally and appeared normal on speculum examination. On rectal examination the uterus was large and edematous. Only 3 of 24 mares were positive on bacteriological culture of the uterus. On postmortem examination the endometrium was very edematous. Knudsen indicated that rarely these mares recovered without therapy, and conceived after being barren for one to two years. There is no specific treatment for lymph stasis but uterine massage and hot saline infusions have been recommended. If persistent CL with high plasma progesterone levels are a possible cause, injections of prostaglandins or a uterine infusion might be helpful in a few cases but the prognosis is poor.

Endometrial cysts in large numbers have been described and may be associated with periglandular fibrosis and cystic distention of uterine glands. Some individual cysts or lymphatic lacunae may be small, 1 or 2 mm. or large, up to 4 or 10 cm. in size that may be found by careful palpation especially if the uterine wall is atrophied.^{9,11,237} They may be mistaken for a chorionic vesicle and pregnancy on palpation or ultrasonography early in gestation, 20 to 35 days.^{157,168b,187} These may be differentiated from pregnancy by repeated examination and finding that the chorionic vesicle grows rapidly while endometrial cysts enlarge very slowly.

Segmental aplasia of the equine uterus is rare.^{195,247}

Lesions of the cervix and vagina are rare in the mare. The most common lesion is an acquired occlusion of the cervix with adhesions due to severe irritation of the cervix at the time of foaling, from severe infectious cervicitis, or from the use of irritating procedures and drugs that produce a severe cervicitis. Mild obstructions may

be broken down and a pessary introduced and left in place for 2 to 4 weeks until healing has occurred.^{172,190} A recurrence of the adhesion across the cervical lumen is not uncommon. **A double cervix and vagina** and a band in an incomplete double cervix in 2 mares was described.²⁹¹

A segmental aplasia of the paramesonephric duct resulting in a missing cervix and a small uterine horn was reported.²⁴⁷ In this case the ectopic ureter entered the antero-lateral wall of the vagina. The author has observed a young Standardbred filly with an ectopic ureter that opened into the lateral wall of the vestibule and resulted in constant dribbling of urine from the vulva. Also rarely seen in the cervix of the mare are ampullary diverticula or cysts, homologues of glands of the male ampulla.^{6,210}

A condition described as a **congenitally short incompetent or hypoplastic cervix** has been described to the author by a number of veterinarians and reported in the literature.⁴³ These young 2-year-old fillies, usually Thoroughbreds, have a severe persistent pneumovagina despite a correctly performed Caslick operation. These fillies have normal-sized ovaries with follicular activity. The cervix is very short, 1–2 cm. compared to a normal cervix of 5 to 8 cm. and is relaxed and widely dilated allowing the examiners hand to enter the uterus, which was normal on fiberoptic examination and on culture and biopsy although a slight endometritis was present.⁴³ The blood progesterone level was 7 to 8 ng/ml. indicating an active CL. The prognosis in these cases is poor for the future breeding life of the filly particularly if the condition is congenital. A somewhat similar condition of a dilated cervix has been reported in fillies with chromosomal abnormalities and in occasional mares during the winter anestrus period. Further study on this condition is indicated.

Cysts of Gartner's duct or remnants of the mesonephric or Wolffian duct in the floor of the vagina are rarely observed.^{6,210} Previously mentioned was the severely lacerated, scarred or incompetent cervix that cannot close properly; affected mares are infertile or sterile.

Persistence of a Portion of the Hymen is not unusual in maiden mares. It is usually ruptured at the time of service. (See Figure 150.) Some veterinarians advise rupturing it with a vaginal speculum 1 to 2 months before service so it is healed before a natural service.^{124,227} In rare cases an imperforate hymen is noted in a maiden mare and requires incising to release the mucus and epithelial debris trapped in the vagina and uterus. Occasional tenesmus may be exhibited in these mares, with a slight protrusion of the distended hymen between the vulvar lips. Occasionally a severe vaginitis or vestibulitis may result in a stenosis of the vulvovaginal border.

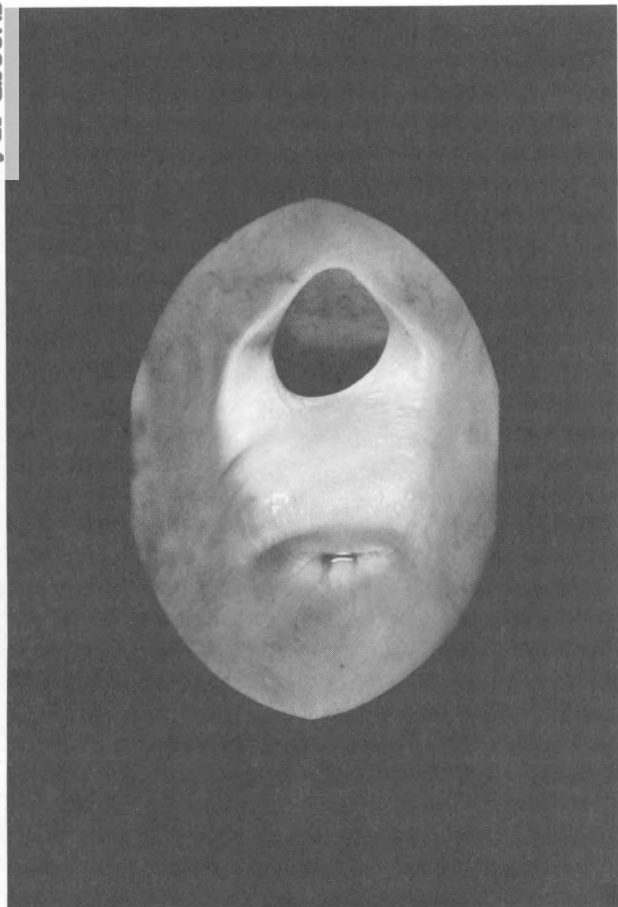


Figure 150. Persistent Hymen in a Filly (Note the urethral orifice caudoventral to the hymen.)

It is not uncommon to note on speculum examination varicose veins in the hymenal folds. Occasionally one of these may break down and a chronic slow dripping of blood may be observed from the vulva. This is most commonly seen in late gestation in fat old mares after exertion. Bleeding is slight and not serious. These mares despite the owner's concern do not abort. Cautery of ulcerated varicosity or ligation may be performed. Usually the intermittent bleeding ceases after foaling.

Congenital Defects, Developmental Arrests, and other anomalies of the reproductive system of the mare are rare. **Hermaphroditism** has occasionally been described and is usually characterized by a large, protruding clitoris and irregular sexual symptoms. (See Figure 37.) McEntee cited Levens (1911) who described 15 cases of male pseudohermaphroditism in stallions descended from the same sire.

There is some evidence to show that certain Thoroughbred female lines, as in cattle, are characterized by infertility of a hereditary nature resulting in a particular mare's female descendants being "shy breeders." The relative importance of this factor requires more scientific appraisal.

Evaluation and Assessment of a Mare for Fertility

This evaluation is routinely required of barren mares at the end of the breeding season on all farms. It may also be requested by a prospective purchaser of a broodmare or a maiden mare.^{22,120,128,130,132,239} This evaluation examination should be thorough and detailed. The interpretation of many of these assessment procedures and final decision requires experience, skilled training, excellent laboratory support, careful observation, excellent records and common sense. Generally one should assess or predict the fertility of a mare in a percentage range or as excellent, good, fair or poor. The veterinarian should seldom indicate a mare is hopelessly sterile unless the severity of the pathological lesions warrants such an extreme opinion. Furthermore the number of examination procedures and their cost should be considered in reference to the value, economic or sentimental, of the mare and the expected breeding costs, such as service, boarding and transportation fees. All mares to be examined for fertility should be carefully identified and all specimens taken from them for laboratory tests should be carefully labelled. A routine procedure of evaluation should be followed and conducted in a professional very clean or sterile manner that poses no danger to the mare or the operator. Careful, complete records should be kept during the examination.

The various factors to consider in this fertility evaluation or assessment include:

1. **Reproductive history**—This should include the animal's age, use, prior illnesses, surgical operations, nutrition, worming and vaccination, practices, and drug therapy, especially the steroids. The pertinent information on number and date of foalings and foaling problems, number of live offspring, and if the mare is barren should be noted. The length of this latter condition, history of services either by AI or natural to what stallions, prior possible exposure to venereal diseases like CEM or infected stallions, history of uterine infection and treatment, teasing and service records, endometrial biopsy report, history of early embryonic deaths or abortions and possible causes, ge-

netic or hereditary background of familial infertility and etc. should be recorded.

2. **Physical or clinical examination**—The mare's physical condition, obese or thin, state of health, presence of an infectious disease(s), examination of the body systems such as teeth, eyes, hair coat, locomotor, circulatory, respiratory and nervous systems for conditions that could affect her fertility or ability to carry, deliver and nurse a foal are necessary to carefully ascertain.
- 3a. **Genital organs**—**Visually examine** the mare externally for the presence of a vulvar discharge, the length, thickness and angle of the vulvar lips and conformation of the perineal region and tailhead that might indicate the presence of or need for a Caslick's operation for pneumovagina. Examine for vulvar or perineal scars, or tumors. **Visual or speculum examination** of the vestibule, hymenal region, vagina and cervix for the presence of a hymen in maiden mares, scars, stenoses, vaginal or cervical exudate, color and condition of the vaginal mucosa, pale, pink, red or inflamed moist, dry and character of mucus, and the external cervical os, the relaxation or edema of the latter should be conducted. These changes may indicate the stage of the estrous cycle or indicate the presence of intrauterine infection (See fibroscopy).
- 3b. **Manual palpation per vaginam and rectum** of the mare's genital organs is necessary. The former examination should further check the external tubular genitalia. The index finger should be gently inserted into the cervix to determine cervical competency and the possible presence of adhesions, scarring or stenosis. The rectal examination should be performed carefully and thoroughly noting and recording the size of the ovaries, presence and size of follicles, the ovulation fossa and any abnormalities such as parovarian cysts, adhesions, tumors, hematomas, varicosities and etc. The uterus should be palpated for pregnancy, or twin conceptuses. If non-pregnant the size, shape, tone, thickness, width and any irregularities or abnormalities of the uterus such as adhesions, endometrial cysts, uterine dilations, edema, atrophy, excessive small size, or mucometra, or pyometra should be noted. The cervix should be palpated for size, width, length and tone. The uterine tubes are seldom palpable in the mare. The size and shape and any abnormal conformation of the pelvic cavity or pelvic bones should also be noted.
- 4a. **Bacteriological culture** of the uterus of barren mares should be taken, especially if a uterine discharge is observed, to determine the organism and its sensitivity to various antibiotics. This test is complementary to the endometrial biopsy examination if evidence of an endometritis is noted on the latter test. This examination should be performed in such a manner as previously described so a true evaluation of the presence or absence of infection is determined. Occasionally repeated cultures may be required. The uterine culture is superior to the cervical culture. In mares with a history of a chronic infection with *Klebsiella* or *Pseudomonas* or to check for CEMO (*Hemophilus equigenitalis*), the urethra and clitoral fossa and sinuses should also be cultured, possibly repeatedly.
- 4b. **Cytological examination** for the presence of leucocytes can be performed on smears from the uterine culture swab.
5. **Biopsy examination of the endometrium** requires a suitable-sized specimen, properly preserved and sectioned, examined and evaluated by a skilled, experienced pathologist or veterinarian trained in this area. The interpretation of the results of both the endometrial culture and biopsy requires an understanding of the findings and their limitations.
6. **Other examinations or tests** that may be helpful or necessary include:
 - a. **Fiberoptic or endoscopic examination** (fibroscopy/hysteroscopy) of the cervix and uterus for the presence of adhesions, cysts, tumors, fluid accumulation, fibrosis and etc.^{22,184,239}
 - b. **Ultrasound examination** of the uterus and ovaries for pregnancy, cysts, follicles or exudate or mucometra.
 - c. **Endocrine assays** for progestins, estrogens, luteinizing (LH) and follicle stimulating (FSH) hormones and prostaglandin metabolites. The former is used most often to determine a persistence of the CL associated with prolonged anestrus.
 - d. **Chromosome analysis or cytogenetic study** of the mare's karyotype is a definite value in certain infertile maiden mares.

The final prediction or assessment of a mare's future reproductive status should also consider the managerial factors and competence of the breeding farm personnel as well as the fertility of the stallion to whom the mare will be bred.

Infertility, "Repeat Breeding." Early Embryonic Deaths and Early Fetal Loss or Early Pregnancy Wastage in Mares

Since infertility and "repeat breeding" in cattle has been studied intensively, much information of general value from these studies can be utilized in developing hypotheses to explain early losses in horses. Limited studies of this area of concern, other than those of a statistical or retrospective nature have been made on mares.

In a large survey of Quarterhorse and Thoroughbred farms the pregnancy rate for the first service period was about 45 to 50% and the cumulative rate for the breeding season was 75 to 85 percent.^{64,268} If only healthy fertile mares were bred to healthy, highly fertile stallions these percentages would probably rise about 10 percent considering the limited length of the breeding season of mares. It is estimated that early embryonic or fetal losses after pregnancy is established as 5 to 8% before the fourth month and 8% thereafter including stillbirths.⁶⁴ On certain farms in certain years early pregnancy loss may occur in 10 to 30% or more of the mares and the cause is seldom ascertained.^{18,52,64,251}

In an excellent retrospective study¹⁸ of 639 Thoroughbred mares on one farm with 2466 coverings in 1528 mare years, the fertilization failure and early embryonic death rate based on a return to estrus within 30 days of a previous cover was 31.7%. While the late embryonic death rate of 26.5% was based on a return to estrus after 30 days after a previous cover (9.4%) and a diagnosis of nonpregnancy at 42 days, often after the end of the breeding season (17.1%). In this study evidence was presented that indicated few "missed" or "silent" estrous periods occurred. But the data suggested that prolonged persistent CL, together with the short breeding season, may have played a significant role in the high incidence, 26.5%, of late embryonic deaths diagnosed at the time of pregnancy examination at or after 42 days post service. The average live foal per cover rate on this farm was 39.8% and the observed late abortion rate was 2.3%. Mares bred late in the breeding season after May 15th had a slightly better foaling rate per cover than mares bred before that date, 44.4 vs 39.0%. Mares bred before 16 days postpartum or on foal heat had a fertilization failure and early embryonic death rate of 40% and a foaling rate of 29% compared to the next or second normal heat of 25.5 and 49%, respectively. Statistics for lactating and nonlactating mares were nearly similar. Foaling percentage for mare age groups of 2 to 4, 5 to 7, 8 to 13, and 14 years and over was 85, 71, 63, and 45%, respectively. This decline in fertility as mares became

older was reflected in the foaling rate per cover, 57 to 25%, combined fertilization failure and early embryonic death rates, 27 to 37%, late embryonic death rates, 15 to 34%, and observed abortion rates 1.2 to 3.1%, respectively, for the youngest and oldest groups of mares.¹⁸

Infertility or "repeat breeding" in cattle is probably due to three major categories, failure of fertilization, early embryonic death and uterine disfunction (See Chapter XIII). Failure of fertilization is characterized by the occurrence of regular intervals between estrous periods while early bovine embryonic death if it occurs after 14 to 16 days postservice often results in a prolonged interval between the time of service and the next estrous period. In mares a similar effect may be noted or the CL may persist even if failure of fertilization of the ovum or very early embryonic death occurred before day 12 post service. This phenomena of persistence of the CL is common to the mare and increases the need for early accurate pregnancy diagnosis. Furthermore, mares that abort after 40 days of gestation when the endometrial cups have developed usually fail to show estrus for a number of months and often not that breeding season. Early embryonic or fetal loss or abortion in mares prior to 90 to 120 days of gestation is seldom observed and may be due to resorption of the embryo or the early fetus within the genital tract. The efficient natural mechanism in most mares that eliminates one of twin embryos early in gestation greatly minimizes the infertility associated with twinning. (See abortion in mares.) In the mare the round to oval small chorionic vesicle of early pregnancy may be expelled rapidly and unseen compared to the cow that has an elongated vesicle that may occasionally be seen hanging from the vulva between 20 to 80 days of gestation. No discharge or blood is observed at the vulva in most mares that abort early. Thus in the mare a regular postservice teasing routine should be followed for several months or more. Errors in early pregnancy diagnoses causes an apparent elevated early embryo or fetal loss. When a pregnancy diagnosis is in doubt repeated examinations either manually or with ultrasonography or even blood tests for PMSG should be conducted as too early incorrect pregnancy diagnoses may contribute, along with inadequate teasing procedures and disease incidence, to an apparent increase in pregnancy losses on certain farms.

Thus management including improper teasing and breeding procedures and erroneous pregnancy diagnoses²⁵¹ may contribute significantly to an apparent increase in early pregnancy wastage. Other management factors may include **nutrition** since one study showed that restricted energy intake between 25 and 31 days of

gestation caused a high incidence of early embryonic loss.²⁹² This loss may be related to the losses of embryos and fetuses caused by stress factors discussed under causes of abortion in mares (Chapter V). In cows and ewes heat stress particularly around the time of fertilization of the ovum and a few days thereafter cause definite large embryo losses and "repeat breeding." This factor has not been studied in mares. Another managerial factor in broodmare management that results in a probable increase in early embryonic losses is the **breeding on foal estrus**. In two studies conception rate on foal estrus was 39 and 41 percent compared to the second estrus after foaling which was 55 and 65 percent.^{18,173,268} However, the abortion rates after the two breedings were similar 16.5 and 13.8 percent, respectively in one of the studies.¹⁷³

A uterine infection, such as CEM, and occasionally *Klebsiella*, *Pseudomonas* or even *Streptococci*, introduced into susceptible mares at the time of service by the stallion may cause an acute endometritis and a "hostile" environment for the spermatozoa and fertilized ovum. The estrous cycle may also be shortened due to luteolysis of the CL by the released prostaglandin. These uterine infections must be prevented or controlled to avoid early embryonic deaths and infertility. Endometritis resulting from the introduction of miscellaneous organisms at the time of service particularly in the infection-prone, usually older mare¹⁸ may also cause early embryonic or fetal deaths.

Endometrial pathology particularly periglandular fibrosis, lymphatic lacunae, large endometrial cysts, endometrial atrophy, hyperplasia and degrees of endometritis often in older mares as revealed by a biopsy of the endometrium is a cause of infertility and early embryonic death. Pregnancy losses in three studies were 10 to 20 percent in Category I mares with essentially a normal endometrium and 35 to 44 percent in Category III (abnormal endometria).^{92,154,251}

Chromosomal abnormalities as a cause for early embryonic loss in the horse is probably the same as in other animals and man. In sows about 10 percent of all ova or 30 percent of released ova that fail to develop had chromosomal anomalies, mainly triploid blastocysts probably due to polyspermy.¹⁸⁸ A similar incidence of chromosomal anomalies, 36 percent, occurs in spontaneous abortions in women.⁷² Although further studies, which are difficult in the mare, are indicated evidence has been presented⁴⁶ of the probable role of chromosomal abnormalities in early embryonic or fetal deaths in horses based on the relative frequency of chromosomal defects in adult horses. The high incidence of mosaicism in sex chromosome anomalies in mares¹³³ indicates that aging of the ovum before fertilization, which

is probable in certain mares due to the long estrous period and uncertainties in the time of ovulation and breeding, results in post-fertilization errors of mitosis.⁴⁶ Also the maternal age effect on the incidence of chromosomal anomalies of the embryo, fetus and newborn commonly seen in women may also be a factor in the incidence of this condition in horses.

In 39 attempts at recovery of embryos from infertile older (16 to 28 years) mares only 10 embryos (26%) were collected compared to an embryo recovery rate of 76%, 119 embryos in 156 attempts in fertile younger, 3 to 15 year-old mares. Since pregnancy rates from embryo transfers from infertile and fertile mares were similar, the lowered reproductive efficiency in the infertile mares appeared related to **failure of fertilization and transport** through the uterine tube, probably due to retention of unfertilized ova in the tube which is common in mares.¹⁴⁸

Although further studies are needed clinical evidence has been presented that **certain infertile stallions** may have twice the early abortion rate of fertile stallions used on the same group of mares.^{52,53} In some instances as cited previously this may be due to certain genital infections carried by certain stallions but it may also be due, as in bulls, to chromosomal defects in the fertilized embryo. Apparently normal semen from infertile bulls has been shown to result in a much higher rate of failure of fertilization than similar appearing semen from fertile bulls (See Repeat Breeding in Chapter 13). A similar condition might exist in horses.

Two further causes of early embryonic or fetal deaths are **twinning** and **trauma to the chorionic vesicle and embryo** by rectal palpation for the early diagnosis of pregnancy. This latter occurrence is probably uncommon in mares over 40 to 45 days of gestation when palpated in a careful gentle manner. However palpation at 15 to 30 days should be done very gently by an experienced operator to avoid possible damage to the embryo or chorionic vesicle. Twinning has been discussed by Ginther.^{117b} Although further studies are needed, it is evident that the mare, in which double ovulations of fertile ova are common, has a well-developed biological embryo-reduction mechanism for the elimination of excess embryos early in the gestation period. Thus factors that contribute to a mare's (or a band of mares) failure to conceive or produce a live foal include the following.^{130,132}

- A. Factors over which the veterinarian often has limited or no control:
 1. Selection of broodmares and stallions is usually based on athletic ability rather than reproductive performance.
 2. The breeding season starts before the physio-

logic breeding season of mares and is shortened by human mandate.

3. Culling of aged, relatively infertile mares and stallions.
 4. Possibly non-selective breeding of mares on foal heat, especially late in the breeding season.
 5. Use of artificial insemination.
- B. Factors over which the veterinarian should have supervisory or direct control:
1. Teasing procedures and practices including visual and manual palpation of the genital organs to overcome behavioral anestrus or continuous or long estrus and prolonged or persistent CL with anestrus in mares; and aberrant sexual behavior in stallions.
 2. Abnormal or pathologic conditions of the reproductive organs including endometritis, pneumovagina, other genital infections, endometrial fibrosis, adhesions, tumors, chromosomal defects and etc. in both mares and stallions.
 3. Nutrition, housing and breeding practices as well as worming and vaccination programs for mares, stallions and foals.
 4. Accurate, complete up to date reproductive and preventive health recording system.

Breeding Farm or Stud Management

Management practices on breeding farms are basically similar to those described for cattle. The veterinarian and stud manager and/or owner must work closely together in a program designed for the farm to secure the highest number of mares pregnant at the end of the breeding season. These pregnant mares should be handled so that they will produce normal, live, strong foals. A goal of over 80 percent conception in the band of mares is considered a satisfactory goal on most farms raising racing stock where the breeding season is short and some of the stallions and mares being used as sires and dams are not highly fertile. Conceptions below 60 to 70 percent are definitely unsatisfactory and require remedial measures.

In a study of reproductive efficiency on 14 horse farms encompassing 6 breeds and a total of 1876 mare-years, conception, foaling, and weaning efficiency averaged 80.1, 73.8 and 70.8 percent, respectively. It was significant that on 2 farms using pasture breeding, conception rates were 94 and 100 percent. The conception rates were very low in February, 27.8 percent, and rose in May through July to a peak of 57 to 59 percent and declined thereafter. Conception efficiency in young mares

fluctuated until age 7, reached a peak at age 9 of 89.6 percent, remained on a plateau above 70 percent until age 15 and declined thereafter. Conception rates on 5 Thoroughbred farms ranged from 53 to 80 percent and on 5 Quarterhorse farms from 72 to 92 percent.¹⁴⁶

Every effort should be made in the Fall to examine, assess or evaluate the reproductive status, treat, if necessary, and outline a plan of breeding of all barren mares for the coming spring season. Infected mares should be treated and cured or eliminated well before the breeding season. Infertile mares and especially maiden mares should be booked to the most fertile stallions. Barren mares that have failed to conceive in a number of years should be culled. The use of increased lighting for barren mares should be considered to prolong the physiologic breeding season. Incorporating artificial insemination using extender containing antibiotics in breeds permitting registration of foals conceived in this manner and using a program similar to the described minimal contamination technique has been helpful in getting more barren mares to foal. If a stallion's conception rate is low his semen should be examined carefully on a number of occasions during the breeding season or preferably before the season. If a stallion is of low fertility, his book should probably be reduced and close attention should be paid to having the mare bred within 24 hours before ovulation. The time of breeding may be determined by careful rectal palpation or the use of HCG. Foaling mares should be properly cared for during foaling, given exercise and examined critically before being permitted to breed on the foal estrus. Teasing all barren, foaling or recently bred mares on a regular daily or every other day basis before and during the breeding season is essential. If this is not done regularly a veterinarian should examine the mare's ovaries for the presence of a mature Graffian follicle and impending ovulation on the same frequent 48-hour schedule. Frequent speculum examinations or services should be avoided especially on the infection-prone mare.

Breeding shed hygiene and restraint should be thorough and on a routine basis. The external genitals should be carefully washed and rinsed. Excessive use of disinfectants on a stallion's genitals should be avoided. Care should be taken not to have disinfectant on the stallion's penis at the time of service. Mares with Caslick operations should be carefully supervised and the number of services should be reduced to the bare minimum consonant with good conception rates. The use of HCG to promote and hasten ovulation may be helpful in these and other older, infection-prone mares. The stallion's semen should be examined to determine if ejaculation occurred and to observe the quality of the semen. If artificial insemination is employed this should be carefully

supervised, monitored and performed in a clean, sanitary manner.

Careful, continuous and complete daily and even lifetime records on all animals and aspects of the breeding program must be kept up-to-date, accurately and in an easily accessible form. These records should be analyzed for each stallion and for the mares during and at the end of the breeding season. All the breeding history, treatments, services, teasing, pregnancy and genital tract examinations must be recorded. A variety of breeding record forms have been devised and used by veterinarians and managers of stud farms. Daily record and permanent record forms are essential. Satisfactory record forms may be purchased from The Lifetime Horse Record Company, 6060 South Broadway, Littleton, Colorado. Records used by Andrews and McKenzie and Beeman were excellent.

The mares and stallions must be on a balanced ration²⁴⁸ and maintained in good condition being neither too fat nor too thin. Mares at the time of breeding should be in a positive energy balance on a rising plane of nutrition. Daily exercise is essential for all breeding stock. It has proven to be a helpful practice, if it is possible, to allow a fertile stallion to run at pasture with barren or infertile mares if infection or other contra-indications are not present.

As in cattle careful and constant attention to many and all details by the veterinarian and the farm manager are essential to a successful reproductive program. Vaccination, worming and other measures are essential for a good foaling rate and the limiting of losses of newborn animals.

It is "unfortunate" that the breeding season of racing mares does not extend from April 15 to September 15, instead of the present February 15 to June 15 in the northern latitudes. The conception rates on many farms would probably rise 10 to 20 percent by this accommodation to the physiologic breeding season of the mare.

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Chapter XV

INFERTILITY IN FEMALE SWINE

The incidence of infertility in sows may approach that seen in cattle. Because of their lower value and the difficulties of diagnosis and treatment, sterility in sows has not been studied as much as has infertility in cattle or horses. The farrowing rates in over 50,000 matings of sows and gilts in the Midwest was about 72 percent.⁸¹

The incidence of sterility in a herd where brucellosis was present was 21.9 percent in 382 sows over 1354 breeding seasons. This varied from 13.9 to 36.9 percent in various breeds.¹¹⁹ Currently the incidence of brucellosis in swine herds in the U.S. is greatly reduced. Five percent of sows and gilts were sterile, another 5 percent were hard to settle, and another 10 to 15 percent showed some impairment of fertility by a small litter size due to high intrauterine death rate of the embryos or fetuses.¹⁰⁴

On postmortem examination 1.4 percent of 1000 sows and gilts were completely sterile and another 2.2 percent had lowered fertility.⁶³ Because swine are multiparous or polytocous, complete sterility in swine is lower in incidence than in cattle but reduced fertility is common.⁸³ In 250 sows, 42, or 16.8 percent, failed to conceive or farrow. Of the rest, 84 percent conceived on 1 service, 12 percent after 2, 2.5 percent after 3, and 1.5 percent after 4 services.¹¹⁹ Several studies showed that litter size rose to a peak at the fifth to sixth litter and then decreased. Ten percent of female swine were sterile.¹⁰⁵ The most common causes of sterility were hydrosalpinges and cystic ovaries; these two pathological lesions accounted for about one-half of the obvious failures to conceive.

Stillborn pigs were classed as a form of infertility.⁸³ Stillbirths occurred in 259, or 23.1 percent, of 1121 litters. Litters of over 12 pigs had an incidence of 11.7 percent stillbirths, while medium-sized litters had an incidence of only 3.9 percent.⁹⁸ The birth weight of stillborn pigs was higher than that of normal pigs. An incidence of 6 percent stillborn, occurring usually in large litters, old sows and in spring farrowings, was reported.⁶ Stillborn pigs were more common in the latter half of the litters as they were born or in those fetuses nearer the apex of the horns. Attempts to hasten parturition with oxytocin gave inconclusive results. According to the literature the incidence of stillborn pigs is 8 to 9 percent. The mortality in the two sexes was about equal.⁶

Sow productivity or piglets per sow per year weaned is based on ovulation rate, fertilization rate, embryo loss and fetal and newborn losses. The farrowing interval, as in cattle, is based on conception rate and lactation length and other possible genetic and environmental factors.^{29,76}

Physiology of Porcine Reproduction

Puberty occurs in gilts at 6 to 7 months of age with a range of 4 to 9 months. Spring born gilts reach puberty 1 to 3 weeks later than gilts reaching puberty during the winter months. High environmental temperatures result in delayed puberty and an increased incidence of anestrus. In contrast to other species the age of the gilt was more important than weight, nutrition or "flushing" on determining the onset of puberty or number of ova released.^{76,80,81} Puberty may be delayed slightly by inbreeding or severely restricting the TDN or protein intake to one-half recommended amounts. It may be hastened by crossbreeding and by allowing boars to contact the gilts.¹⁶⁹ Moderately cold temperatures, and transport or environmental stress also hastened the onset of puberty. Certain breeds of swine such as the Landrace reach puberty earlier, 160 to 180 days, than other breeds, 200 to 230 days. Length of daylight or exposure to artificial lighting had no effect on reproductive cycling or puberty in sows or gilts.^{81b} Gilts that have not reached puberty by 240 days of age should be culled. Exogenous hormones were of limited value in promoting estrus in prepubertal gilts.⁷⁶ Total confinement significantly reduced the proportion of gilts attaining puberty by 9 months since about 25 percent were noncyclic and of these one-third were prepubertal and one-half were behaviorally anestrus.^{23,24,81} The greater the number of estrous cycles after puberty and before service in gilts, the greater is the ovulation rate.^{33a}

There is enough FSH and LH in the pituitary gland of gilts for several weeks before puberty to cause the onset of the estrous cycle. If prepubertal gilts are stressed by transport or by a marked change in environment, estrus will often occur within 4 to 7 days after the stress indicating the release of FSH. This same period of time is required to produce estrus in prepubertal gilts after the

injection of PMSG. Recurrent estrus may not follow this early induction of estrus and ovulation in gilts. In general, increased amounts of PMSG injected to induce follicle formation and estrus and HCG to induce ovulation results in a greater number of ova released at the induced ovulation. However, there is a great inconsistency in the number of ova released by exogenous gonadotropins injected into different gilts in various seasons, herds and years.^{2,33a} Gilts that reach puberty and conceive at an early age and have 9 or more piglets in the first litter should be retained as brood sows.²²

The estrous cycle—The sow is polyestrous the entire year. Estrus usually does not occur during lactation or for at least 30 days after farrowing. Estrus usually occurs 3 to 7 days after weaning. After 6 to 10 years of age senility may affect the estrous cycle. The estrous cycle averages 21 days in length and may vary from 18 to 24 days.^{2,7,3,29,42,76,144} The estrogenic phase of the cycle is 6 to 7 days and the luteal phase is 14 days with CL regression beginning on day 16. The duration of estrus is 1 to 4 days, with an average of 2 to 3 days, or about 60 hours. Ovulation usually occurs between 24 to 42 hours, or an average of 36 hours, after the onset of estrus. Nearly all sows examined had ovulated by 40 hours. Older sows have a slightly longer estrous period and cycle than gilts. Failure of ovulation results in a longer estrous period, and premature ovulation will shorten the period. Ovulation is spontaneous in sows. It takes about 4 to 6 hours from the rupture of the first follicle to the rupture of the last follicle. The LH surge in gilts and sows is about 20 hours long and peak LH plasma levels immediately preceded or were coincident with the onset of behavioral estrus in 60 to 70 percent of the sows. However in about 20 percent of the sows the LH surge was delayed for 18 to 24 after the onset of estrus. This variability may explain the lowered fertilization and conception rates in certain sows where frequent checks for estrus and services per estrus are limited. Sows should be checked for estrus 2 or more times per day and bred every 18 to 24 hours after the onset of estrus for 2 or more services.^{153b} Ovulations are slightly more frequent, 51 to 55 percent on the left than on the right ovary. The size of the follicles at ovulation is 0.7 to 1 cm. in diameter.¹

Small follicles are present in the porcine ovary during diestrus, but during proestrus and estrus although approximately 15 to 40 follicles approach maturity only about 10 to 20 ovulate. From 7 to 16 days after ovulation the corpora lutea are at their maximum size, about 1 cm. in diameter.¹ The weight of the ovary during diestrus may reach 8 to 10 gm. Degeneration of the corpora lutea is rapid just before and during the next estrus and a few

days before and after parturition.

The symptoms of estrus in the sow are definite and usually marked.^{2,3,7,29,42,58,59,76,142} The sow has a reduced appetite and is restless and nervous, often pacing back and forth by the fence. Salivation, champing of the jaws, and frequent grunting may be pronounced. The sow, if suckling, may ignore her pigs; may try to escape, or if free will seek out the boar and stand for service. During estrus the vulvar lips become swollen and congested and the mucous membrane is pinkish-red in color. Some mucus may be present at the vulva. The most noticeable feature of estrus in the sow is her grunting and standing motionless for long periods in a position for service. This peculiar, immobilizing reflex or stance can be produced in over half of the estrous sows by the pressure of the hands on the sow's back or by straddling the sow. In the presence of the boar with his characteristic odor, his grunts or acoustic signals, and his pushing and lifting of the rear parts of the sow by placing his snout between her rear legs, this sawhorse-like immobile stance and acceptance of the boar will be induced in nearly 100 percent of estrous sows. In late estrus or early metestrus, a whitish mucous discharge composed of mucus, cellular debris and leucocytes may be seen on the vulva.⁷ The vaginal smear or the body temperature do not produce an accurate indication of the stage of the estrous cycle.⁸⁵ As in the other domestic animals changes in the conductivity of vaginal mucus will predict the time of estrus but will not pinpoint the time of ovulation in gilts.³⁹ The vaginal epithelium in the sow undergoes cyclic thickening during estrus when it has 8 to 15 cell layers. During diestrus this will decrease to 4 to 5 layers and during pregnancy to 2 to 3 layers. This permits vaginal biopsies to be utilized for the diagnosis of pregnancy in swine.^{33a} The musculature of the uterus and oviduct is most active during estrus. The endometrium and especially the region where the uterine tube enters the uterus is quite edematous. In healthy sows and gilts 90 to 100 percent of ova are fertilized and 80 to 90 percent of sows farrow after service to a fertile boar.

Plasma hormone concentrations or levels during the estrous cycle have been determined by radioimmunoassays (RIA).⁷⁶ Estrogens are fairly low, 8 to 12 pg/ml except during estrus, days 18 through day 1 of the next cycle when they peak at about 30 pg/ml. Plasma progesterone levels are 1 ng/ml or below during estrus but rise rapidly after ovulation to 20 to 30 ng/ml from days 7 to 16 of the cycle and then decline. Prostaglandin levels in the uterine vein rise to 6 ng/ml between days 14 to 16 of the cycle. Plasma LH has a number of lesser small peaks during the cycle but rises to the highest peak or preovulatory surge of 4 ng/ml at the onset of estrus

between days 20 and 1 of the next cycle. Plasma FSH concentrations are about 6 to 7 ng/ml during the cycle but rise slightly on days 21 to day 4 of the next cycle. Estrus and ovulation are inhibited by estrogens and progesterone. Prostaglandin F_{2a} can induce luteolysis of CL but swine CLs are refractory to prostaglandins until day 12 of the cycle.⁷⁰ So the use of prostaglandins to synchronize estrous cycles in sows or gilts is impractical because they are only effective days 12 through 15 of the cycle. The value of PMSG to increase ovulation rate is negated by the high prenatal loss of embryos so litter size is relatively unaffected.^{42,76} HCG and GnRH if administered late in proestrus or at the onset of estrus will induce ovulation in about 40 hours.⁴² The principal urinary estrogen in sows is estrone. The peak in urinary estrone excretion occurred just before estrus.

Estrous signs can be induced by estrogen injection in ovariectomized sows or in sows without functional corpora lutea. However, if estrogens are injected into sows with mature corpora lutea during the luteal phase of the cycle, estrus does not occur. In fact, even a single injection of estrogen into sows at this period will prolong the life of the corpus luteum causing anestrus that may persist for a number of weeks. Thus, indiscriminate use of stilbestrol or estradiol in sows to promote estrus is to be avoided.^{33a,60}

About 60 to 90 percent of sows will exhibit signs of estrus 2 to 3 days, range 1 to 5 days, after farrowing and will accept the boar.^{2,42} If sows are bred at this estrus they do not conceive because ovulation rarely occurs.^{8,160} Furthermore if a few ova are shed and fertilized they do not develop. This estrus might be due to estrogens from the ingestion of the placenta at parturition.⁵ The older usual or traditional lactation period in sows was 56 days (8 weeks). This period is being shortened to improve sow productivity. The uterus of the sow is completely involuted within 21 to 28 days after parturition. The uterine weight decreased from 2.8 kg on the day after farrowing to 0.2 or 0.3 kg at 21 to 28 days.¹¹³ Most sows that are suckled go into a lactational anestrus that lasts for 6 weeks or longer or until the pigs are weaned. Sows whose litters were weaned at 10 days after parturition came into estrum more than 9.4 days later, 2 sows developed cystic ovaries, and only 12.8 ova were released at the first estrum. Sows whose litters were weaned at 21 days came into estrum at an average of 6.2 days later, and ovulated an average of 15.2 ova. Sows whose litters were weaned at an average time of 56 days, came into estrum an average of 4 days later and ovulated an average of 16.6 ova.⁶⁶ The earlier after farrowing piglets were weaned to produce early cycling and concep-

tion the longer the time from weaning to estrus and the lower the conception rates and smaller the litter size. However if pigs were weaned at 21 to 28 days,^{81b} or possibly 35 days³⁹ sow productivity for the year was maximized. Sows came into estrus sooner after weaning than gilts and white breeds sooner than black breeds.⁷⁶ About 60 percent of primiparous sows returned to estrus the first week after weaning compared to 85 percent of multiparous sows. During the summer, postweaning anestrus, up to 4 months, in the former is increased; only 65 to 75 percent of sows were in estrus the first week after weaning. This delay was more apparent in primipara. Shade and evaporative cooling had little effect. Weaning to estrus interval was shorter because of reduced stress in crossbred sows and in crated sows than in sows penned in groups.^{80,81a,b}

Synchronization of Estrus—During lactation and suckling estrum does not occur. But after the pigs are weaned estrum usually develops in about 4 to 9 days or an average of 5 to 7 days.^{33a,42,76,85,139} Under some circumstances, when it is desirable to synchronize the breeding and farrowing dates, estrum may be produced in a lactating sow by removing her pigs each night for 4 to 5 nights and allowing the pigs to nurse during the day,¹³³ or by weaning the pigs at 3 to 5 weeks of age. Lactation may be suppressed by the former practice. Some sows, if fed well and with a boar nearby come into estrum 5 to 7 weeks after farrowing even with pigs still suckling.¹⁶⁴

Synchronization of estrus in gilts and sows can most practically be accomplished by management procedures. Introduction of boars into close contact with gilts along with transport or a change in the environment to produce stress will usually initiate estrus within a week in puberal gilts. In sows synchronization can also be accomplished readily by weaning pigs after 3 to 5 weeks of lactation and the introduction or close contact with boars. Increasing the nutritive level or "flushing" for 4 to 8 days with 3 to 4 kg/day of a well-balanced ration may slightly improve the ovulation rate.⁷⁶ Vasectomy for heat-check boars has been described where artificial insemination is desired.⁶² Teaser-gilts to be used for detecting sows in estrus could be produced by long-time injection of testosterone propionate¹³⁵ as has been demonstrated in cows and ewes.

Over the past twenty years much research has been conducted with progestins, the gonadotropic hormones, PMSG and HCG, methallibure and recently GnRH alone and in various combinations to induce synchronized estrus in gilts and sows to aid in artificial insemination at a specific time to progeny-tested boars. The results have

varied widely.^{74,131,162} The routine use of PMSG in the U.S. is negligible because of its limited availability even though it has been shown to induce ovulation in lactating sows. Recent studies indicate that estrus synchronization in the future might be possible.^{74,127,146a} Altrenogest (allyl-trenbolone) fed orally at a dose level of 15 to 40 mg./day for 14 or 18 days to gilts effectively synchronized estrus. Low doses of this progestin caused cystic follicles.^{90a,146a}

Ovulation, Fertilization and Ova Transport—The rate of ovulation is 10 to 15 ova and 12 to 20 ova for gilts and sows, respectively. A slightly higher rate of ovulation may occur in certain breeds, in crossbred gilts and in sows 2 to 4 years of age. Very low ovulation rates, 4 or below or very high ovulation rates as in superovulation may result in the loss of the entire litter.¹⁶⁶ Markedly restricting the energy intake will decrease the ovulation rate but this can usually be promptly restored by feeding a high level of TDN, or "flushing" for a week or more depending on the condition of the sow. High rates of ovulation result in larger litter size at 25 days of gestation. But at farrowing the litter size is not increased by higher than normal ovulation rates.^{33a}

In Wrathall's review it was shown that the greater the ovulation rate the lower the prenatal survival rate. Losses of embryos in the pre-attachment stages, before days 15 to 17 of gestation, are mainly due to inherent limitations within the embryos themselves. While in the post-attachment stages losses are due mainly to limitations imposed on the conceptuses by the uterus basically involving uterine length or capacity and the evenness of distribution and spacing of the blastocysts. Those conceptuses with inadequate attachment areas for the diffuse porcine placenta either die or are growth retarded. About 10 percent fetal loss from 30 to 40 days to term is due to uterine space limitations.¹⁶⁶ Thus even though ovulation rates might be elevated by various means, litter size remains fairly constant for the breed and age of the sow or gilt.^{33a,76,166} If large litters of over 12 pigs are born the death losses in these litters prior to weaning are higher. Most embryonic or prenatal losses occur before 25 to 30 days of gestation when the blastocyst begin to elongate rapidly at 11 to 18 days and when attachment is occurring at 18 to 40 days. Thus there is about a 65 to 75 percent embryo survival in most porcine pregnancies based upon ovulation rates of 10 to 22 ova and 8 to 12 pigs born per litter.⁷⁶ Included in these losses are lethal genetic factors causing up to 50 percent of the losses in the blastocyst stage^{95,96} and losses due to possible maternal effects including abnormal uterine secretions ("milk") between days 9 to 16 of gestation. The admin-

istration of progesterone or progesterone and estrogens to augment early embryo survival has not resulted in a conclusive or consistent beneficial response.^{33b,76} High levels of energy or TDN during gestation is not necessary or desirable as early in gestation it may increase embryo loss and late in gestation cause increased size of the fetus, and birth and postpartum problems.

The best time to breed or inseminate sows or gilts is 24 hours apart on the first and second day of estrus or about 12 hours before ovulation which occurs about 40 hours after the onset of estrus.^{42,78} Sows bred the day before heat, the first day of heat, the second day of heat and the third day of heat had 9.8, 68.8, 98.2 and 15.2 percent fertilized ova, respectively.⁷² The average number of fertilized ova in sows mated at the proper time was 95.5 percent. Factors affecting the fertilization and conception rate are boar fertility, timing of service and seasonal conditions, or heat stress.⁷⁶ Sperm cells were present in the uterine tubes of sows within 15 minutes of breeding. Thirty minutes after breeding, although 30 to 60 billions of spermatozoa were in the uterus, only about 90 to a few hundred spermatozoa were in the uterine tubes.^{53-56,76} Seminal plasma and spermatozoa were rapidly lost from the uterus and phagocytosis of sperm cells began within a few hours after mating. Although both live and dead cells may enter the uterine tube, the live sperm cells remain motile in the tube for 24 hours while those in the uterus showed a greatly reduced motility after 2 hours. A mass of live sperm cells accumulate at the uterotubal junction in the apices of the uterine horns for 24 hours and then decline during the next 24 hours thus providing a steady flow of sperm cells through the junction into the uterine tube. The fertilizing ability of swine spermatozoa lasts only 25 to 30 hours in the sow.⁸⁵ The best time to breed sows was 10 to 25 hours after the onset of estrus. If the sow is bred the first day of estrus she should be rebred the second if she is still in standing estrus.

When ovulation time was controlled by an injection of HCG during proestrus and gilts were inseminated 2 hours before ovulation and 2, 6, 10 and 14 hours after ovulation, the proportion of CL represented by normal embryos at 25 days of gestation were 73, 61, 53, 28 and 32 percent, respectively. In control gilts bred 6 hours before ovulation, 88 percent of the CL were represented by normal embryos at 25 days of gestation.^{77a} Aging of ova and spermatozoa significantly affected the number of surviving embryos at 25 days.⁵⁶ Twenty-six percent of sows bred 44 hours after the onset of estrus had heteroploid embryos 17 days later probably due to polyspermy. Four percent of heteroploid embryos were observed.

Fertilization in female swine must take place in the ampullae before 60 hours after the onset of estrus to cause conception and before 50 hours to produce cytologically normal embryos.¹⁵ The block or zona reaction in the vitelline membrane in the ova to polyspermy is highly effective when the sow is mated the first half of estrus.^{33a,76,78}

Thus, it would appear from the above data that capacitation of spermatozoa must occur before fertilization. Fertilization can occur within 2 to 3 hours after insemination. The corpus luteum develops steadily requiring a full week for development.⁵ Fertilized ova in swine pass through the first half of the uterine tube very rapidly and remain near the ampullary-isthmic junction for 24 to 39 hours or until 60 to 75 hours after the onset of estrus. The fertilized ova at the 4-cell stage of development pass into the uterus about 44 to 54 hours after ovulation or 66 to 90 hours after the onset of estrus.^{42,112} Thus swine ova enter the uterus sooner than in the other domestic animals. The morula stage develops and the zona pellucida is shed in the apices of the uterine horns 6 to 8 days after the onset of estrus.^{33a} The blastocyst grows very rapidly from 4 mm. in diameter on the 9th day of gestation to 110 cm. in length on the 16th day.¹¹⁷

Intrauterine migration of fertilized zygotes occur during days 9 through 12 just before the rapid elongation of the blastocyst or blastodermic vesicle^{42,78,159} in sows and has been confirmed by comparing the number of CL in each ovary with the number of embryos in the corresponding horn. Although 55 percent of the CL were on the left ovary, each horn contained 50 percent of the fetuses.⁹² In sows that are unilaterally ovariectomized before mating or sows in which one uterine tube is ligated, equal numbers of embryos implant in each horn.¹⁵⁹ It has been estimated that 40 percent of the zygotes migrate from one horn to the other. This was also shown by ova transplantation.^{41,44} This is apparently accomplished by the motility and activity of the uterine musculature to assure both efficient distribution and equidistant spacing of each embryo. The pig blastocyst synthesizes estrogens from about day 12 of pregnancy. This is apparently responsible for the maternal recognition of pregnancy in this species as estrogens increase blood flow to the uterus and have a luteotropic effect on the corpus luteum. This increased blood flow may explain why luteolysis is not produced by the uterine prostaglandin in early pregnant sows.^{57b}

Litter size—Much study has been conducted on causes of reduced litter size. The prenatal mortality in swine has been estimated to be about 45 percent.¹⁴³ Most of these losses of zygotes occur during the first 25 days of gestation. About 6 percent of these losses occur in late ges-

tation and at parturition resulting in stillbirths. Gilts bred the first, second and third estrus after puberty have 6.9, 8.0 and 9.4 pigs per litter, respectively. In another trial this difference was not significant in well-grown gilts.¹⁶⁸ Farrowing rates also increased from 83 to 94 percent from the first to third estrus after puberty.^{80,81,168} There is an increase in prenatal mortality with increased age of the sow and parity because the increased ovulation rate in sows is not associated with a similar increase in litter size. The peak in litter size occurs about the 5th to 7th litter or 2 to 4 years of age.^{5,33a,137,138} The decline in litter size in older sows is due to an increase in embryonic death rate.

Heritability of litter size is low, 10 to 15 percent.^{16,33a} Litter size will differ between breeds by an average of 3 to 4 pigs per litter. This difference in litter size between breeds may be associated with an increased ovulation rate in certain breeds.⁴⁷ Inbreeding of the dam causes a decrease in litter size and crossbreeding an increase in litter size due to heterotropic effects.^{13,33a,80,81} Embryonic mortality may also be a characteristic of the individual sow. The sire of the sow is also an influencing factor.¹¹⁵

Each of 27 boars in two studies^{141,147b} were mated with about 10 gilts and it was found that boars exerted a significant effect on conception rate ranging from 30 to 100 percent. The number of live embryos at 25 to 30 days of gestation ranged from 3 to 17 with an embryonic survival rate of 24 to 84 percent. If a boar had a conception rate below 65 percent this could be an important cause of reduced litter size.¹¹⁴ Thus culling boars with low conception rates would improve fertility in the herd and increase litter size.^{141,147b} Chromosomal abnormalities have been described in a significant percentage of embryos from normal sows as a cause of infertility or reduced litter size.⁹⁵ One boar was reported that had normal semen volume, sperm cell numbers and progressively motile spermatozoa but had a zero impregnation rate when mated to 12 sows.^{147b} In this instance nuclear or sperm head defects or chromosomal abnormalities might be suspected.

Litter size is usually larger in spring farrowings than in fall farrowings. One disadvantage to multiple farrowing in sows is the lowered fertility in the summer months. Hurtgen reported that farrowing rates are 15 percent, range 2 to 40 percent, lower in the summer, July through September, than in the winter months. Many infertile matings had a delayed interval or return to estrus indicating possible early embryonic death or abortion and mimicking viral reproduction failure.^{80,81} Sows stressed by exposure to 85 to 100°F. heat from days 1 to 5 or 15 of gestation had an increase in embryonic death rates.^{45,80,81,154}

If the sows were stressed by heat before breeding or from 15 to 30 days of gestation, there was no effect on embryonic death rates. Thus, cooling sows with sprinklers on hot days may be indicated the first week or two after breeding. Severe cold stress did not affect litter size.^{147a} Stress due to transportation or change or environment has not been reported to effect fetal mortality.

Confinement of gilts had no effect on the farrowing rate compared to those bred and maintained in outside lots. Furthermore mated gilts maintained in gestation crates in one study had a 13.8 percent higher farrowing rate.⁸¹ There is no evidence that exposure to light over a range of 6 to 18 hours has any effect on ovulation or conception rates in female swine.

Mating on 2 consecutive days of estrus by the same boar improves farrowing rates by 10 to 25 percent in sows and 10 to 13 percent in gilts. When a different boar is used for the second mating farrowing rates increased an additional 4 to 8 percent, respectively, but litter size only increased 0.2 pigs/sow.^{28,80} Sows bred once during an estrum had a 68 percent conception rate and sows bred twice had a 78 percent conception rate. Two services produced 0.5 to 0.7 more pigs per litter than once service.¹⁴⁷ There was no significant difference in the number of ovulations and litter size in sows bred the first or second estrus after weaning their pigs.^{137,138}

The quantity of uterus affected the uterine capacity to maintain fetuses. When one horn and ovary was removed from 59 gilts the litter size at 25 days of gestation was similar to the intact control gilts, but at 105 days of gestation the treated gilts had 5.5 fetuses in the single horn compared to 9.4 fetuses in the intact gilts. In a large number of gilts it was demonstrated^{41,42,44} that intrauterine crowding was not important in early embryo survival at 25 days or 30 days and only when a gilt had 14 or more oversized embryos did it appear likely that uterine crowding was a possible limiting factor in embryonic survival. After transferring 16 to 28 fertilized embryos to gilts, the litter size was similar to control gilts, 8 to 10 pigs.¹⁰ Thus, uterine capacity is an effective factor in limiting litter size. This effect apparently occurs after day 40 of gestation.

A high level of nutrition or energy intake in gilts and sows for several weeks prior to breeding and during the breeding period results in slightly higher ovulation rates.⁸⁹ The level of feeding has no effect on fertilization but a high level of energy intake for four weeks after conception results in a variable but greater embryonic mortality depending upon the amount of energy given. This may possibly be related to heat or other stresses. Limited feeding of female swine is indicated following breeding.⁷³ The number of pigs born is not affected by the

plane of nutrition as long as it is adequate during the latter two-thirds of gestation. The level or quantity of protein is not as critical as energy in its effect on reproduction. Most swine nutritionists recommend 5 to 10 percent alfalfa in the ration during gestation to promote normal farrowing of healthy well-grown pigs. Sows should be kept in lean or moderate condition during gestation for economic reasons and to avoid dystocia or farrowing problems common in fat sows or gilts.

Although both progesterone and estrogen are needed to produce a proper intrauterine environment for the growing embryo, there has been no evidence that implants or daily injections of progesterone and estrogen at a ratio of 2000:1, or single injections of either hormone have any beneficial effect on embryonic mortality.^{33b,34}

It has been suggested that uterine infections during the breeding period and shortly after conception may account for a reduction in litter size. The evidence supporting such a factor limiting litter size is present but not conclusive.^{35,100,131,140} Feeding chlortetracycline and tetracycline continually or only during the breeding period produced no significant benefits.^{35,140} The author and others²⁹ recognize the contradictory reports on the effects of antibiotics fed at the time of breeding on reproduction, but recognize that in a herd acutely-infected with leptospirosis or a similar bacterial infection, antibiotic treatment during the gestation period may be beneficial in reducing fetal mortality and stillbirths. (See Chapter V).

The 30 to 40 percent deaths of fertilized ova or early embryos characteristic of pregnancy in swine, and the other species, may well be nature's way of eliminating some unfit or abnormal genotypes at a low biologic cost. The incidence of genetic or congenital abnormalities in the newborn is low because most are eliminated early in pregnancy.

The utero-ovarian relationship in swine is similar to cattle and sheep. Hysterectomies performed in sows the first half of the estrous cycle caused prolonged anestrus and the maintenance of corpora lutea for the approximate duration of gestation, about 110 days. If the operation is performed late in the cycle, ovulation occurs and the subsequent corpora lutea produced persist for a similar period. If nearly all of the uterus is removed from non-pregnant sows leaving only a portion that is less than one-fourth the length of the horn, then the CL will regress only on the side of the retained small portion of the horn; the CL on the opposite side will persist. If the portion of the uterine horn left in place is one-fourth the length of the uterine horn or longer then the CL will regress on both sides because sufficient amount of prostaglandin is released from the endometrium to cause in-

volution or regression of the corpora lutea. Thus in swine if there is a blind horn due to a localized segmental aplasia involving only a portion of the horn so that zygotes are present only in one horn, then prostaglandin released in the nonpregnant horn or segment of that horn will cause CL regression and prevent implantation and pregnancy. If one horn is ligated near its base, and the sow is bred at estrum, the developing zygotes will not be present in that horn and the prostaglandin will be released resulting in a regression of the CL and the onset of estrum terminating the early, unicornual, pregnant state. If one horn and its corresponding ovary are completely removed then pregnancy can occur in the remaining horn. Thus an intact, but nonpregnant horn will cause CL regression on both ovaries in swine but not in cattle.^{4,36-38,61,97}

Once pregnancy is established with zygotes throughout the uterus the prostaglandin release is suppressed and cycling ceases and corpora lutea persist.¹²¹ By day 14 to 15 at least 4 viable embryos or more are necessary in gilts to suppress prostaglandin and maintain luteal function during early pregnancy.^{78,122} When all the fetuses or embryos in one horn were killed between 4 and 50 days of gestation, that pregnancy was maintained in gilts so treated between 12 and 50 days, but was not maintained in gilts so treated from 4 to 10 days of gestation.^{37,38,110} In these latter gilts the CL regressed on both ovaries. Thus after day 13, pregnancy will continue even if all of the fetuses in one horn die or become mummified. The author has observed a sow with all of the fetuses mummified except one and pregnancy was maintained. (See Figure 74.)

Anatomical, Congenital, and Possibly Genetic Abnormalities of the genital tracts of female swine are occasional causes of failure of conception which can be explained by the close utero-ovarian relationship previously described that results in early regression of the CL induced by the release of prostaglandins before day 12 of gestation in the uterine horns not containing developing embryos. Of 19 "repeat breeding" sows and 44 "repeat breeding" gilts 5, or 11.4 percent of the gilts had a unilateral missing segment of the uterine horn, or uterus unicornis.¹⁶¹ Nineteen, or 43.2 percent, of the gilts and 2, or 10.5 percent, of the sows had bilateral tubal abnormalities; 2, or 4.5 percent, of the gilts had bilateral missing segments such as a missing vagina, cervix, or body of the uterus. Animals with bilateral tubal abnormalities were included with those having hydrosalpinx, "pyosalpinx", and bursitis. Present in the broad ligaments of some of the gilts were structures that appeared to be rudimentary ducts or remnants of the mesonephric or Wolffian duct system. With so many abnormalities affecting gilts, the logical conclusion was that they were developmental defects or arrests. Of 79 female swine that

had been bred an average of 2.8 services without conception,^{105,107,165} a unilateral missing segment was found in 1 gilt and 1 sow, or 2 percent and 3.6 percent, respectively. A unilateral blind segment was present in 4, or 7.8 percent of the gilts, and 1, or 3.6 percent, of the sows. A blind uterine body was found in 1, or 2.0 percent, of the gilts, in many cases the blind horn was distended with mucus. One gilt had a missing cervix. Another 354 day-old gilt had infantile reproductive organs with a complete lack of estrous periods. In several cases one uterine horn, uterine tube and ovary were missing. In cases in which one horn, usually the left horn, and the adjacent ovary were missing, pregnancy occurred normally in the other horn but the litter size was reduced by about one-half. A partial doubling of the uterine horns was observed in 5 of 500 gilts.³⁶ Some of these became pregnant and farrowed. This might be genetic in nature. In Belgium it was reported that 2.2 percent of 1000 female swine examined had missing segments of the uterine horn; 3 percent of the gilts had hydrometra; there were 4 cases of a uterus didelphys (double cervix); and 1 had a missing uterine body.⁶³ A case of uterus didelphys and other cases of a double cervix and median septums of varying lengths in the vagina located most commonly near the hymen and extending cranially were described.^{102,150,158} After examining 2967 gilts and 1288 sows, the following incidence in slaughter house material of missing and double parts of the genital tract was reported.¹⁶³

	Percent
Missing uterine horn	0.3
Missing segment of uterine horn	0.3
Missing vagina, cervix, and uterine horns (with male ducts in broad ligaments)	0.02
Missing cervix	0.02
All reproductive organs missing except vulva	0.04
Double cervix	0.04
Double uterine horn	0.02
Total	0.74

There were 1.8 percent of the open gilts, 0.6 percent of the pregnant gilts, and 1.2 percent of the open sows—or a total of 1.5 percent of 5088 sows and gilts—with tubal abnormalities. None of these abnormalities, except possibly a missing vagina or cervix, could be diagnosed in the living animal by practical methods. Thus it was emphasized by the above figures that anatomic arrests in development were not uncommon.¹⁶³

Of these anomalies hydrosalpinx was the cause of the greatest amount of sterility. Anatomic defects were found in 21.5 percent of the sterile female swine examined.^{105,107,165} Thirty three percent of "repeat breeding"

swine had bilateral tubal abnormalities.¹⁶¹ The incidence of defects in sterile gilts in these reports was 31.3 percent and 43.2 percent, respectively. In sows the incidence was much lower, only 3.6 percent and 10.5 percent, respectively. Of 142 or 3.3 percent genital tract anomalies in 9250 gilts and 9 or 1.8 percent anomalies of the genital tract in 476 sows, about one half were either segmental or total aplasia of the paramesonephric ducts.¹⁵⁰ Thus in swine, especially gilts, anomalies of the genital tract are not uncommon. The incidence is definitely higher than in other species of farm animals. Hermaphroditism in swine is seen occasionally and the affected animals are usually male pseudohermaphrodites, (See Chapter III).

Tubal abnormalities are common in swine in the U.S. as noted above but uncommon in Europe.^{105,107,150} They are usually bilateral and probably genetic in origin and result in hydrosalpinx or "pyosalpinx." In sterile female swine, usually gilts, 35 percent had obstruction of the uterine tubes. In hydrosalpinx, which was by far the most common lesion, there appeared to be an obstruction in the lumen of the uterine tube about two-thirds of the distance from the ovary to the horn, causing an accumulation of fluid.^{161,165} They reported that bursitis, or adhesions between the fimbria and ovary occur commonly in cases of hydrosalpinx. These adhesions were probably secondary to mycoplasmosis, polyserositis, peritonitis or intraperitoneal injection of an irritating substance in piglets.¹¹ Twenty or 2 percent of the 1000 female swine examined had bursal adhesions. These apparently are not so common or serious as the hydrosalpinx that may be associated with them.⁶³ Occasionally "cysts" of the bursa developed secondary to severe adhesions. In hydrosalpinx, which was very common, 97 percent of the cases were bilateral and usually the uterine third of the tube was involved or obstructed.¹⁶⁵ In some cases the uterine tube was patent and a light yellow bacteriologically-negative material was flushed with some force from the lumen. This would effectively prevent the passage of spermatozoa and ova. In most cases of hydrosalpinx or "pyosalpinx," adhesions of the fimbriae to the ovaries were present. There was some evidence that these hydrosalpinges and "pyosalpinges" might have been caused by the obstruction of the uterine tube by embryonal rests of the Wolffian duct system.^{105,107} The condition was invariably bilateral and showed some tendency to be inherited. It appeared almost entirely in nulliparous gilts. Attempts were unsuccessful to reproduce this condition experimentally in normal females by inoculating their uterine tubes with contents from affected tubes. Whether hydrosalpinx and adhesions are due to disease, to congenital lesions, or to some other factors is not definitely known. More work is needed on this problem.

Pathological Lesions or Diseases of the Reproductive System in swine, besides those mentioned, are cystic ovaries and inflammations of the genital tract. The former will be discussed later under hormonal causes of sterility. Nonspecific postpartum or postservice metritis is not considered as common in the sow as in the cow and mare; retained placenta is of less frequent occurrence; delayed involution of the uterus with endometritis, a common cause of postpartum sterility in cattle, is not common in sows. Only two cases of pyometra have been described.^{63,165} On examination of 5088 sows and gilts, no gross uterine infections were reported.¹⁶³

In Chapter XI the mastitis-metritis-agalactia (MMA) syndrome or "milk fever" in sows was discussed. This acute condition occurs soon after parturition and has been the subject of much recent intensive research. The disease MMA has largely been described as a clinical entity characterized by a degree of lactational failure oragalactia also associated with signs of anorexia, stiffness, fever, swollen mammary glands and the usual postpartum mucoid vaginal discharge. Infertility has not been described following this MMA syndrome.^{5,130} The postpartum vaginal discharge is usually not associated with a uterine infection.

Specific Infections of the Genital Tract causing sterility in swine include brucellosis caused by **Brucella suis**. The uterine lesions of brucellosis in swine are well described.¹⁵¹ Often the only recognized symptom of brucellosis in swine is an increased incidence of infertility.⁸³ In one brucella-infected herd 37 of the first 100 sows bred failed to conceive. Eight naturally infected sows studied over a 2-year period farrowed only 14 litters, even though bred for 2 litters a year. Of the 129 pigs born in these 14 litters, 44 were stillborn and 17 were weak and died within 2 days of birth, a loss of nearly 50 percent. In another herd, having 80 percent reactors to the brucellosis test and much sterility, 3 gilts were slaughtered; all had a purulent cervicitis and metritis from which **Br. suis** was recovered. In "repeat breeding," brucella-positive, female swine the incidence of embryonic death was 87.5 percent as compared with an incidence of 46.5 percent in brucella-negative females.¹⁶¹ When sows infected with *Brucella* were serviced by a fertile boar the pregnancy rate was only 35 percent compared to 90 percent in uninfected gilts.¹⁵⁷ This infertility was due to macroscopic and microscopic lesions of the endometrium causing early embryonic deaths with prolonged periods between heats. When infertility is a problem in a herd of swine, the brucellosis status of the herd should be determined.

A boar with **Staph. aureus** infection of the vesicular glands bred 18 females and only 4 conceived, 3 conceived subsequently to another boar, 3 were sold as ster-

ile, and the remaining 8 sows developed an acute metritis with a vaginal discharge. Two of these 8 sows were rebred later and aborted.⁵¹ On postmortem all showed a chronic metritis resembling that due to brucellosis. During a 3-week period 8 of 209 7-month old virgin gilts developed an acute severe metritis due to *Staph. aureus* with an elevated body temperature and copious vaginal discharge.⁴⁹ There is no evidence that leptospirosis causes sterility in swine, even though there is much evidence that it may cause abortions. A high incidence of defective pigs and early embryos and mummified fetuses were reported in non-immune sows vaccinated against hog cholera with the modified virus vaccines 10 to 16 days after conception.^{40,167} Other viruses described in Chapter V including picorna viruses, Aujeszky's disease (Herpes) virus, parvovirus ("SMEDI") and several other viruses described in Japan will cause heavy pre-natal mortality.⁴⁰

Coital vesicular exanthema, or vesicular venereal disease, may in rare cases affect the caudal portion of the genital tract of sows and gilts.^{8,84} This has not been described, and if present is probably rare, in the United States.

Several cases of a **ruptured cul-de-sac** of the cranial and lateral portion of the vulva after copulation were described.¹⁶⁵ These lesions were apparently caused by penetration of the vulvar mucosa by the penis. They were inflamed bulb-like structures containing coagulated blood. Intromission was apparently painful and was resented. In many instances the affected females, even though in estrus would often refuse to accept the boar. Sometimes the female would have a normal service followed by evidence of pain at subsequent services. These lesions did not cause permanent sterility and did not affect the more cranial portions of the genital tract.

Vulvovaginitis, characterized by swelling of the vulva with a mucous discharge, enlarged mammary glands and occasional prolapse of the rectum has been described in Chapter V. This condition is due to the feeding of moldy corn or barley in which estrogenic compounds, zearalenone, were present. Zearalenone (F-2) is an anabolic estrogen-like mycotoxin produced naturally by *Fusarium* growing in grains stored under high moisture conditions. Feeding of this mycotoxin caused infertility with small ovaries and atretic follicles and no corpus lutea and squamous metaplasia of the epithelium of the genital organs. It also caused nymphomania, pseudopregnant sows with persistent corpora lutea, juvenile hyperestrogenism in nursing piglets, malformations and possibly fetal resorption.²¹ Swollen reddened vulvas were reported in pigs consuming a poultry feed containing dienestrol. These animals exhibited estrous behavior. The isolation of a

mycotoxin from *F. graminearum* (*Gibberella zeae*) that caused vulvovaginitis, vaginal prolapse, perineal relaxation and ovarian atrophy in young gilts was described.^{91,146} The action of the mycotoxin was identical to estradiol. When the estrogenic metabolite, zearalenone, of *Fusarium roseum* (*Gibberella zeae*), a common mold of corn is present at high enough levels in grain this mycotoxin causes testicular atrophy and rectal prolapse in boars, vulvar reddening, swelling and vaginal prolapse in gilts and nipple enlargement in both sexes. In some nonpregnant gilts zearalenone will cause persistence of the CL, pseudopregnancy and anestrus with edematous uterine horns. Moderate doses fed to pregnant gilts caused decreased weights of the uterus, placental membranes and fetuses.^{48b} High levels of moldy feed fed 3 to 34 days of gestation caused inhibition of fetal development and decreased numbers of fetuses.^{92b,168b} Other trichothecene mycotoxins such as deoxynivalenol produced by *F. roseum* have also been associated with reproductive disorders, infertility and abortion in sows.^{92b}

Hormonal or Endocrine Disturbances are described as being responsible for about 4 percent of the infertility in female swine or 20 to 50 percent of infertile sows. This is the second most common cause of infertility in swine. A 24 percent incidence of cystic ovaries in 821 sows was described and 83 or 10 percent of these sows were sterile.¹¹⁶ Occasional follicular or luteal ovarian cysts were found in all stages of pregnancy, as well as in nonpregnant sows and gilts.^{105,106} In pregnant sows, cysts apparently developed or persisted after conception inasmuch as ovulation in nonpregnant, cystic females rarely if ever, occurred. The presence of these cysts in pregnant sows was not related to litter size and did not interfere with gestation. Estrus and service may occur during pregnancy in sows possibly associated with the development of follicles or the presence of high levels of estrogen. Cystic ovaries in pregnant female swine could invariably be produced by a single injection of a small dose of 200 to 400 IU of PMS. Cysts on ovaries in pregnant sows was not observed.¹¹⁶ About twice as many cysts, 35 percent were noted during the spring months as in the fall months, 15 percent.

The incidence of cystic follicles in ovaries with corpora lutea was 1.1 percent and cystic follicles alone was 0.6 percent of 5088 female swine.¹⁶³ Cystic ovaries were reported with corpora lutea in 7.6 percent and with no corpora lutea in 2.5 percent of 79 infertile or sterile sows.¹⁶⁵ Six percent cystic ovaries with corpora lutea and 3.2 percent cystic ovaries with no corpora lutea were observed in 63 "repeat breeding" sows.¹⁶¹

Cystic ovaries in nonpregnant swine were of 3 types—

single cysts, multiple, large cysts, and multiple, small cysts.¹⁰⁴⁻¹⁰⁶ Single cysts were found in 2 percent of 1751 pairs of ovaries. In these cases only 1 or 2 cysts were present on the ovary. They were 2 to 3 cm. in diameter, whereas a normal follicle is only .7 to 1.1 cm. in diameter. The reproductive tract and behavior of these female swine were normal. These single cysts were found during the luteal phase of the cycle with normal corpora lutea present. These were probably atretic follicles that failed to rupture when ovulation occurred and were not associated with sterility.^{104-106,116}

Multiple cysts were always associated with permanent or temporary sterility. Three to 4 percent of non-pregnant females were affected. It is usually impossible to differentiate clinically between sows with large or small multiple cysts as estrous cycles in both are irregular and characterized by anestrus periods of varying length.

Large multiple luteal cysts were most common. These measured 2 to 10 cm. in diameter and an average of 5.6 cysts were present on each ovary. Thus the number of these cysts was nearly the same as the normal number of follicles. The walls of these large cysts were either heavily luteinized or contained lutein patches. The uterine endometrium in these cases showed progestational changes. The external symptoms manifested by these sows were extreme irregularity of the estrual cycle with intervals of 2 to 90 days between estrous periods. The heats were of greater intensity but of the same duration as those in normal noncystic females. In 60 percent of the affected female swine the clitoris was larger and longer, up to 1 to 2 cm. in length, than the clitoris of normal females, 1 to 2 mm. in length. The amount of estrogen present in these large cysts was less than in normal ovarian follicles. Androgens were not present. Although progesterone was present, the amount could not be measured. It was believed that progesterone, or progesterone converted into androgens, was the probable cause of the enlarged clitoris. There was no significant difference between the gonadotropic activity of the hypophysis in cystic and noncystic sows. In sows with large cysts given injections of LH, neither ovulation or further luteinization of the cysts resulted. This does not mean that LH deficiency might not be the cause of the condition, as the animals treated had been affected for a long period.^{104-106,116}

Small multiple follicular cysts were observed only occasionally. They resembled a cluster of grapes and were always present in numbers exceeding the number of follicles found normally. These cysts were about 1 cm. in diameter. An average of 22.5 small cysts per ovary was reported.¹⁰⁴⁻¹⁰⁶ The walls of these small cysts were lined by normal granulosa cells. The uterus showed an estro-

genic type of endometrium and the clitoris was not enlarged. These animals showed marked irregularities in the length of the estrual cycle. Symptoms of estrus were intense, similar to the symptoms produced by the larger cysts. In neither large nor small multiple cysts was nymphomania, or continuous estrus, observed. These small cysts were found to be as rich in estrogen per unit weight as the normal follicles, but because of the large number of small cysts the total concentration of estrogen was 4 to 5 times that of the normal ovary just before ovulation and several hundred times that of sows affected with large luteal cysts. The pituitary assays showed no increase in gonadotropic hormones over that seen in normal sows. A single small dose of 250 to 400 PMS always produced cystic ovaries in nonpregnant swine but the cysts never reached the size of large luteal cysts.

Thus it appeared that multiple cysts may be due to lack of luteinizing hormone necessary to cause ovulation and normal corpus luteum formation. It is doubtful that sows once they develop cystic ovaries recover spontaneously.¹¹⁶ Whether there is a genetic basis or cause for cysts in sows as in cows is not known. Further work is required to determine the actual cause and possible therapy of cystic ovaries in swine.

Porcine ovarian abnormalities other than cysts include: ovotestes in hermaphrodites, ovarian abscesses, rare parovarian cysts, and aplastic or missing ovaries.¹¹⁶

Anestrus is common in prepuberal gilts and post-weaning sows.^{24,46,79,81a,b,82,86} The incidence of anestrus is most common in the summer months but varies from 20 to 40 percent in both gilts and sows.⁸²

In 54 anestrus gilts 10 to 11 months of age examined at slaughter 19 gilts or 35.2 percent had no luteal tissue in the ovaries and were prepuberal. Forty two percent of the gilts had ovaries with active corpora lutea indicating cyclic activity but the external heat signs either were missed or were too weak to be observed. The remaining 10 gilts, 18.5 percent, had normal corpora lutea and/or luteinized cysts.⁴⁶ In another study of anestrus gilts 7 to 9 months of age, 50 percent exhibited behavioral anestrus and would not mate even when exposed continuously to a boar. These were confinement-reared gilts and estrous cycling was occurring based on plasma progesterone levels at frequent sampling periods. This study also showed that exogenous ACTH and glucocorticoids inhibited estrous behavior and shortened the duration of estrus. Further studies on confinement-rearing stress and managerial practices to reduce this stress is indicated.²⁴ In a third report from Japan⁸⁶ 192 sows or 70 percent of 274 sows with ovarian "disease" were anestrus or failed to exhibit estrus based on rectal palpation of the ovaries under thiamylal sodium anesthesia, 20 ml IV. Thirty

percent of these 274 sows had corpora lutea and 30 percent had cystic ovaries.

The factors contributing to anestrus in swine are prepuberal status or delayed estrus in gilts and sows due to the breed, age, nutrition, season, especially summer, lack of boar exposure, confinement-rearing or management problems, and failure to check frequently several times daily and observe estrus, preservice or postservice.^{79-81a,b} To minimize to problem of anestrus and infertility in a swine herd, it is essential that all non-pregnant sows and gilts of breeding age be adequately "teased" daily by boars that have demonstrated their estrus detection ability and libido. Postweaning anestrus in sows is most common in the summer months, especially in primiparous young sows. During the summer months 40 percent of the fertile matings was followed by a return to estrus in a 25 to 35-day interval. This interval is suggestive of a pregnancy that was present for 12 or more days followed by early embryonic death.⁸⁰ Pregnant sows are anestrus. Boars lacking libido may be a cause of missed estrous periods. Too many sows in a pen for a boar to check efficiently may also be a cause of apparent anestrus. Excessive stress on prepuberal or postweaning females causes anestrus and short estrous cycles. Cystic ovaries, either follicular or luteal cysts may cause anestrus but these are not as common as the other factors. Lactating sows and gilts are usually anestrus. Other causes of anestrus include: delayed puberty is seen more often in Durocs and Yorkshires; first litter gilts are more frequently anestrus than multiparous sows, 35 vs 15 percent; gilts and sows whose pigs are weaned during the summer are more frequently anestrus than those whose pigs are weaned in the winter, 40 vs 10 percent; the larger the number of sows penned together the greater the incidence of anestrus due to the loss of condition and lack of feed intake in some sows; cystic ovaries and lameness also contribute to the anestrus condition as well as inefficient management and failure to detect estrus.^{81b}

Since anestrus is a symptom, an accurate diagnosis is desirable but may be difficult to achieve. Progesterone levels above 1.5 ng/ml on a number, 6 to 18, of affected animals would indicate estrous cycling is occurring, the sow is pregnant or a luteal cyst is present. Serial samples 5 to 10 days apart would aid in diagnosing whether cycling is occurring. Slaughter house or abattoir examination of a selected sample of females in a herd would also be most informative.^{81b} Costly rectal examinations of the ovaries of anesthetized sows, although difficult, could be very helpful.^{86,99}

Treatment of anestrus in gilts and sows, as in cattle, requires as accurate and correct a diagnosis of the cause as possible.⁷⁹ The history, records, physical examination

of the females for pregnancy by ultrasonography at 30 to 35 days of gestation or other means, nutritional status, age, season, managerial practices, disease factors, and other tests as noted above should be carefully reviewed. The use of PMSG for treating anestrus sows was reported in 1953.¹²⁵ Estrogens and HCG gave poor results. Later trials with PMSG also proved promising.^{43,90} In gilts stressing by trucking, movement or mixing of females, introduction of a boar and giving PMSG (500 IU) or PMSG and HCG (250 IU) if no corpora lutea are on the ovaries frequently induces estrus within 3 to 5 days at which time breeding should take place.^{81b}

If corpora lutea are present prostaglandins 5 to 10 mg of PGF_{2a} or 1 mg (100 ug) of a prostaglandin analogue might be used.⁸⁶ They are ineffective except between days 12 and 15 of the estrous cycle or in cases of persistence of the corpus luteum or luteal cysts and could cause abortion in early gestation.^{17,87b}

Prevention of seasonal postweaning anestrus in sows during August through October was accomplished by administering 500 IU of PMSG at weaning. This study reported 52.8 percent of controls and 91.3 percent of the treated sows in estrus within 7 days after weaning during the months of August through October.^{81b,82} Estrus occurred 3 days later about a day earlier than controls. Presently PMSG is not available commercially in the U.S. Further trials with other FSH products are indicated. Ovine pituitary gonadotropin showed promise for the treatment of cystic ovaries in sows.⁸⁶ Repeated daily doses of 5 to 10 mg of estradiol for 5 to 20 days to age the luteal tissue followed 5 days later by prostaglandin to involute the CL and induce estrus has been reported.¹⁷

It was recommended that gilts not in estrus by 8 or 9 months of age and sows anestrus for more than 40 days after weaning should be culled.⁷⁹ A high incidence of anestrus after weaning in one herd was associated with a low packed-red-cell volume of about 20 percent and many sows serologically positive for *Eperythrozoon suis*.¹⁸

In a study of 63 anestrus gilts over 7 months of age and 28 sows that failed to show estrus within 5 weeks of weaning less than 10 percent of the gilts and more than 40 percent of the sows had corpora lutea indicating the presence of an estrous cycle.¹¹⁴ After the stress of transporting the gilts to the study center and changing their environment 68 percent of the gilts and 25 percent of the sows came into estrus within 10 days. Daughters of late maturing gilts were also late maturing so a genetic factor was involved in this type of anestrus that might be susceptible to improvement by selection for early puberty. Rare cases of infantile or hypoplastic ovaries and genital tracts in well-grown gilts have been described.¹⁶⁵

Repeat Breeders in female swine, as in other ani-

mals, are caused by high embryonic death rates and low fertilization rates. These are also causes for reduced litter size. Embryonic death was of more importance than was the ovulation rate in controlling litter size in swine.⁸ Between 10 to 25 percent of sows and gilts fail to conceive.^{104-107,163} In these sterile swine, gross abnormalities of the reproductive tract were the cause of sterility in 25 to 50 percent of the gilts and 25 percent of the sows. In the rest of the sterile females there was no apparent cause for the failure of fertilization or early embryonic deaths. Failure of reproduction due to embryonic deaths appeared less common in gilts than in sows.

In an experiment modeled after those made on "repeat breeding" cattle, 63 "repeat breeding" female swine were assembled.¹⁶¹ These had previously been bred 2 to 4 times without conceiving. They represented 5 breeds and included both gilts and sows. Part of the 63 were killed 4 days after service to a fertile boar and the rest were killed at 25 days. Those that came in estrus again before 25 days were rebred and killed 4 days later. Gross abnormalities were found in 63.7 percent of the gilts and 31.6 percent of the sows. Some of these were unilateral and permitted conception. In the percentage of reactors to the blood test for brucellosis there was no significant difference between either the gilts and the sows, or between those with gross abnormalities and those with no gross abnormalities. The difference in percentage of fertilized ova between brucella-positive and brucella-negative animals was not significant but the incidence of embryonic death was 87.5 percent in the positive animals, and 46.5 percent in the negative animals. This experiment showed the importance of the role of brucellosis in infertility in swine. These workers¹⁶¹ concluded that "repeat breeding" was due to failure of fertilization in 53.4 percent of the gilts and 32.6 percent of the sows. Gross abnormalities accounted for failure of fertilization in 50 percent of the gilts and 16.8 percent of the sows. Thus accountable failures of fertilization occurred in 3.4 percent of the gilts and 16.8 percent of the sows. Embryonic death caused "repeat breeding" in 23.9 percent of the gilts and 67.4 percent of the sows. "Repeat breeding" swine with normal embryos 25 days after the one additional breeding included 22.7 percent of the gilts and none of the sows. Therefore, the major cause of "repeat breeding" in gilts was genital abnormalities causing failure of fertilization. In sows the major cause of "repeat breeding" was embryonic deaths.

In another study 79 "repeat breeding" sows and gilts that had been bred 3 to 10 times previously were assembled.¹⁶⁵ All brucella-positive females were eliminated from the experiment. After being bred to a fertile boar on the first estrus, 53.2 percent conceived. They considered that this high conception rate in infertile females may

have been due to breeding an average of 3.9 times per estrus as compared to only 1.4 times per estrus previously. There was some indication that these animals might have ovulated early. Only 5 to 10 percent of these animals could be considered to have experienced embryonic deaths.¹⁶⁵ This is in marked contrast to the 20- to 70-percent rate of embryonic deaths reported in the previous study.¹⁶¹ The 5 to 10 percent of the animals exhibiting extreme embryonic mortality were apparently fertile but a reduction in litter size occurred soon after implantation. Some of these losses were probably due to segmental aplasia and defects of the uterine horns and genital tract resulting in early and complete loss of embryos.

Repeat breeders could also be due to poor management and infertile boars.¹¹⁴ Of 75 female "repeat breeding" swine brought to the study center and bred the next estrus to a fertile boar, 49 females conceived. The conception rate experienced by "travelling" boars on first service was 62 percent for gilts and 56 percent for sows; in herds using their own breeding boars the respective percentages were 82 and 77. The lower conception rate in "travelling" boars may have been due to overuse, the presence of genital infections, or poorly timed services.

Tumors of the genital tract in female swine are rare, possibly because most swine are slaughtered at a relatively young age. Leiomyomas and a fibroma of the uterus in sows and one case in which a lymphoblastoma involved one ovary have been described.⁵⁰ The author has observed a 12 × 7 × 4 cm. hamartoma on the ovary of a sow. A rare teratoma of the porcine ovary was reported.¹⁰³ Embryonal nephromas and sarcomas of the vagina and cervix have been described.¹⁰¹ Two hemangiomas, a papillary cystadenoma and a granulosa cell tumor of swine ovaries were found.¹⁰⁹ Other reports on ovarian cystadenomas, sarcomas, teratomas and a fibroma have been cited.¹⁰⁹

Nutrition may have a definite effect on fertility in female swine.²⁹ Except for a few important differences, the same general principles apply to swine as to the other farm animals. As in all animals, inanition due to a low plane of nutrition in swine results in a delay in the onset of puberty, and failure of estrus, or irregular estrus after weaning. The detrimental effects on embryonic survival of overfeeding and a high energy intake immediately after breeding have been discussed. The beneficial effects of a temporary high plane of nutrition to promote early puberty and a higher ovulation rate have also been described. Gilts on a protein-free diet failed to cycle normally or conceive.¹ A protein deficiency acute enough to cause severe retardation of growth in sows did not affect the incidence of fetal atrophy.³¹

The presence in newborn swine of embryonic defects

and abnormalities caused by a vitamin A deficiency in sows during early pregnancy has been reported.^{12,69} These anomalies included eye defects or the absence of eyes. Evidence was cited to indicate that deficiencies of vitamin E, C, B, complex and D are seldom, if ever, the cause of infertility in the sow or other farm animals.^{128,129} Evidence of severe deficiencies in phosphorus, calcium or other minerals affecting reproduction in swine have not been reported in recent years.

Reproductive management in swine herds, as in cattle herds, requires close cooperation between the owner and/or the manager and the veterinarian. The success of a reproductive program lies in its day to day efficiency and effectiveness which is primarily the responsibility of the manager and/or owner.^{29,81a,b} The results of several recent large surveys of swine fertility in the U.S. revealed that overall farrowing rates were only 72 percent in over 50,000 sows and gilts. Some well-managed herds achieve an 85 percent farrowing rate. Infertility, sterility and small litter size may be due to a variety of infectious agents and boar infertility discussed in this chapter and in Chapter XVIII, respectively. Other factors contribute to low fertility and should be recognized. Farrowing rates during the summer months, June through September, average about 15 percent lower than in the winter months of November through March in the northern hemisphere. This high seasonal loss of pregnancies is apparently not due to failure of fertilization, boar fertility or infectious agents. The nature or cause of this apparent loss of pregnancies is not known.^{81b} The farrowing rate of gilts is lower than first-litter gilts which is lower than multiparous sows. Crossbred females are more fertile than purebreds. Although high ambient temperatures reduce conception rates and embryonic survival its role in the summer infertility problem is equivocal.^{81b} As the number of females in a pen increases, fertility decreases due to heat detection, nutritional, infectious disease and stress problems. Sows and gilts should be bred twice during estrus at a 24 hour interval and to two different boars for highest fertility. Females should be tested for estrus starting 17 days after mating and checked for pregnancy at 30 to 40 days of gestation with an ultrasonic detection instrument.

In diagnosing or preventing reproductive failures or inefficiencies a number of requirements are essential including:

- 1) Breeding records, necessary to monitor and analyze the monthly (seasonal) and yearly programs and results including the inventory, costs and net income.
- 2) An evaluation and understanding of the standard of management including training and capability of

personnel and herd management procedures, including buildings, animal comfort, degree of stress and techniques for estrous observations and breeding both females and males, and pregnancy testing.

- 3) An evaluation and understanding of the nutritional program including adequacy of TDN, protein, minerals and the delivery of the rations to the herd.
- 4) A good preventive disease control program is essential including vaccinations, parasite control, feed additives, quarantine and isolation facilities and practices, supervision of farrowing and vector control.
- 5) The genetic program and goals of the owner and/or manager should be understood and integrated effectively to improve herd productivity.

To further these goals the veterinarian and owner and/or manager should have a good veterinary diagnostic laboratory and consulting service that also includes a nutritionist, a geneticist, an accountant, and if the herd is large a computer would be desirable. If artificial insemination is to be used in a swine herd excellent management of the female herd, very competent estrous detection, careful control of the boar, semen collection and insemination and complete records are essential.

Standards of production that are recognized as necessary for a successful swine herd operation are:²⁹

Litters/sow/year	2 to 2.25
Pigs/sow/year	20 to 21
Stillbirths (%)	5
Farrowings (%)	88-90
No. of live pigs/litter	10-11
Weaning to service interval (days)	7
Repeat breedings (%)	6-8
Abortions (%)	1.0
No. of pigs weaned/litter	9.5
No. pigs marketed/sow/year	18.0

If these standards or goals are not closely approached or met then it is necessary for all concerned to properly assess their deficiencies, correct the problems and work toward achieving these standards in order to insure the success of the enterprise.

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Chapter XVI

INFERTILITY IN EWES AND DOES

Infertility or sterility in ewes and does is uncommon when compared with the incidence of these conditions in other domestic animals. This is probably true for two reasons: first, there has been less study of the infertility or sterility occurring in these animals; and second, the incidence of disease or infertility apparently is much lower in these species because of their lower economic value and prompt elimination if they are infertile. Fertile members of the species have been selected and perpetuated over many years. In examining the genital tracts of 90 ewes, no structural defects or other abnormalities that would be a barrier to fertilization were found.^{37b} There are many similarities between the genital tracts, the ovaries, the reproductive hormones and other facets of reproduction between ewes, does and cows. The structure and functions of the various portions of the genital tracts of ewes and does are similar to that of the cow, and treatment of pathologic conditions is similar to that used in the cow except for the fact that the smaller size of the ewe and doe renders impossible the use of certain procedures and types of therapy employed in the cow. Because of the differences between the ovine and caprine species in reproductive physiology and to avoid confusion, the author is separating the discussion in this Chapter into two sections—Infertility in Ewes and Infertility in Does.

INFERTILITY IN EWES

Reproductive Physiology

Puberty occurred in spring lambs at a mean age of 249 to 293 days, 8 to 9 months; Rambouillet or crossbred lambs born in the fall had their first estrus at 316 days range 199 to 577 days.^{43,54,159} About 90 percent of the lambs had ovulated before the first standing estrus, as noted by laparotomy and the presence of a corpus luteum. In lambs that were not bred, it was noted that over 53 percent ovulated after the last standing estrus of the breeding season. Many lambs only exhibit one or a few estrous periods their first breeding season. Sexual maturity varies with the breed and rate of growth. The fine-wool or Merino type sheep are slow to mature and often

fail to reach puberty the first breeding season. Early maturing breeds such as the Finn-sheep may reach puberty as early as four months of age.^{3,83} Merino sheep mature more slowly than the Hampshire or Suffolk breeds. Crossbred lambs generally mature earlier than purebred lambs. A high plane of nutrition may hasten the onset of puberty and a low plane of nutrition will delay it as in cattle.¹⁴³ Most ewes are bred at the first breeding season after they reach one year of age. Under good conditions of feeding and management 60 percent or more of spring lambs of the early-maturing breeds will become pregnant if placed with rams in the fall. Virgin ewes were still fertile after reaching 4 years of age¹⁵⁸ this is different from 4 to 5-year-old virgin cattle. (See DeLange.)

The estrous cycle—The common coarse-wool breeds are seasonally polyestrous. The fine-wool breeds like the Merinos, Rambouillet and the coarse-wool horned Dorset and crossbreds of these breeds may be polyestrous the year around, depending upon climatic and feed conditions. The coarse-wool breeds in the northern hemisphere usually come into estrum about September 1. If they are not bred or do not conceive they continue to come into estrum until about January 1 or slightly later. Rambouillets tend to come into estrum the earliest in the breeding season; followed by the Hampshire, South-downs and Shropshires.¹

About 12 to 48 hours after parturition about 10 percent of ewes exhibited estrus.^{61,157} After this brief estrous period probably due to the high plasma levels of estrogen and the low progesterone levels postpartum¹²⁸ lactational anestrus lasting 5 to 7 weeks usually develops. After this period some ewes suckling lambs will exhibit estrus but most heats are not observed until about 2 weeks after the lambs are weaned. As determined by the fern pattern of cervical mucus, lactating ewes have one or more quiet or silent ovulations before the first estrus after lambing. It is very difficult to induce estrus unless an involuting corpus luteum is present or exogenous progesterone is given.^{54,55,105} In sheep, as in cattle, progesterone apparently is necessary to potentiate the effect of estrogen to produce signs of estrus.

When rams were introduced into a flock of ewes at

the beginning of the breeding season, 40 to 90 percent of the noncycling ewes ovulated within 65 to 72 hours. These ovulations were preceded by LH peaks about 35 hours after ram introduction.⁸⁹ This study confirms prior reports that ewes ovulated within 6 days of the introduction of rams early in the breeding season. This first ovulation is not accompanied by signs of estrus. But the next estrus period 17 to 24 days after ram introduction is associated with estrus and fertile copulations. Thus the presence of rams at this time of the breeding season triggers the release of GnRH or LH causing a "silent" estrus with ovulation and CL formation. Although the duration and intensity of estrous signs were similar to ovulating puberal ewes in the same flock, 6 to 33 percent of the first estrus periods of puberal ewes were anovulatory as determined by endoscopy. The following inter-estrous period was of normal length, 16 days.⁴⁸

In a recent study it was shown there are usually two peaks of estrous activity after rams are placed with ewes early in the breeding season, the first at 18 to 19 days and the second at 22 to 24 days.⁹⁰ Frequent laparoscopic examinations revealed that 85 percent of ewes that were previously anovular, had ovulated within 4 days of ram introduction. Premature regression of the CL occurred in 50 percent of the ewes between days 4 and 8 and the first estrus in these ewes occurred at about 23 days after the rams were introduced. The remainder of the ewes ovulating within 4 days of ram introduction had no regression of the CL and they showed their first estrus at 19 days.⁹⁰

In fall-lambing Rambouillet ewes the average interval from lambing to the start of regular estrous cycles was 72 days, range 12 to 212 days; this varied from 46 days for ewes lambing in August to 98 days for ewes lambing in January.⁷ The onset of estrous cycles is hastened by early weaning of lambs. The interval from lambing to breeding had a significant effect on conception but had no effect on the induction of estrus.¹⁵⁴ Apparently, as in cattle, a 40 to 60 day interval postpartum was necessary for an optimal conception rate. Uterine involution is largely completed by 24 days postpartum.⁵² Thus, with the Dorset, Rambouillet, or Merino breeds or their crosses, it is possible, but very difficult on a flock basis, to obtain two lamb crops or a 200 percent or greater lamb crop each year. By alternating breeding in the spring and fall, it would be possible to get 3 lamb crops in two years.⁷⁶ Over a two-year-period 539 Rambouillet ewes were mated for six weeks beginning the 21st of March, the 21st of June the 21st of September and the 21st of December in the northern hemisphere. The incidence of estrus in open ewes for the four mating periods was 84.5, 96.4, 97.2 and 99.1 percent, respectively; the ovulation rates were

105.6 140.8; 175.4 and 151.9, respectively, and the lambing rates were 83.9, 96.5, 126.8 and 135.2, respectively.¹³⁵ The higher ovulation rates in June and September were not reflected in higher lambing rates because the higher environmental temperatures during the breeding season had a detrimental or modifying effect on embryonic survival.

The factors limiting the achievement of the goal of two lamb crops or a 200 percent lambing rate per year in the coarse-wool breeds was reviewed.⁸⁰ The manipulation of light and temperature was not practical because of the long latency period required to induce results.⁸⁰ Although ovulation rates could be increased by: (1) breeding during the middle of the breeding season instead of late in the season, (2) "flushing" the ewes by increasing the TDN or energy intake for several weeks prior to breeding, or (3) by the injection of PMSG, preceded by progestin, 3 to 4 days before the next estrus, or on days 12 or 13 of the cycle, only 20 percent of the ewes with 3 CLs were carrying 3 fetuses while 75 percent of the ewes with 2 CL were carrying two fetuses. Thus although a combination of breeding management, including controlled lighting, and hormonal therapy makes 2 lamb crops per year feasible, much more research is needed to make it practical and a routine procedure for most breeds of sheep.^{91b}

The presence of a ram stimulates the breeding activity or the onset of estrus in ewes in the transitional period between the anestrous period and the breeding season.^{77,78,139,164} As noted previously the first ovulation thus induced is often silent and the next period associated with a regressing corpus luteum that provides some progesterone is manifested by signs of estrus. This technique can be used to obtain a degree of synchronization of estrus in a flock. When rams were introduced from July 1 to August 8th, the maximum conception period occurred 17 to 32 days later.¹³⁹ When rams were introduced after August 8th conception rates for the first and second 16-day periods of the breeding season were similar. If a vaginal pessary containing a progestogen was placed in the vagina of the ewes for 12 days during this transitional period before the breeding season and then removed the day the ram was placed with the flock, over 90 percent of the ewes were in estrus within 4 days and 62.5 percent lambled to first service.^{164,165} Thus combining a progestational agent and the introduction of a ram resulted in a higher level of synchronization. As with boars, the presence of a ram, the senses of smell, sight and contact all combine to produce a stimulation of the onset of the estrous cycle and ovulation in the ewe. This effect was not produced when the ram ran continuously with the ewes.^{77,78}

Photoperiodism is a characteristic of the reproductive cycle or the sexual activity in sheep and goats, and horses.^{3,66,67,101,102,142} The onset of the estrous cycle and the breeding season in most breeds of sheep is principally influenced by the reduction in the length of daylight in the late summer and fall in the northern hemisphere. A reduction in daylight to about 10 or 11 hours, whether it occurs naturally or whether it is induced artificially by penning the ewes in a darkened area during part of the day, will induce the onset of the estrous cycle in anestrus ewes. The seasonal nature of the breeding season permits the birth of lambs at the most favorable time or in the late spring months when feed supply and ambient temperatures are nearly optimal. The breeding season of sheep tends to become shorter at latitudes near the poles.^{3,67} Near the equator ewes tend to have estrous cycles throughout the year and not exhibit a restricted breeding season. However irregular and prolonged intervals between estrous periods due to a persistence of the corpus luteum, especially in June, was reported in Niger Peulh ewes in Africa.^{166a} In the northern latitudes there are year to year minor variations in the onset of the breeding season as in horses. A reduction in ambient temperature occurring naturally or induced artificially also has an effect on promoting the onset of the reproductive cycle and the breeding season.^{39,66}

There is a wide breed difference in the number of estrous periods per year from 2 to 3 periods in a short breeding season in some breeds to estrous periods in other breeds in regions near the equator occurring all the year around.^{3,67} The ram, similar to the stallion, does not show a restricted breeding season as does the female but there are seasonal variations in semen production and characteristics.^{3,67} (See Male Infertility.) Rams are sexually more active and produce better quality semen during the breeding season. The onset of the breeding season could be somewhat advanced by a higher energy intake before the season.^{123,124}

Most breeds of sheep have an average cycle length of 16.5 days, with a range of 14 to 19 days.¹ Most of the breeds are in estrus for a period of 20 to 40 hours, with an average of about 28 to 36 hours and ovulation occurs in estrus about 24 to 27 hours after its onset. If AI is used it is best performed about 10 hours, 2 to 15 hours, after the onset of estrus.¹²⁸ The Texel ewe has two follicular growth waves. The first wave began on days 1 and 2 and ended on days 11 to 12 but atretic changes were evident beginning on days 5 to 6. The second growth wave began on days 9 and 10 and resulted in mature follicles at the next estrus.³³ Thus these changes were similar to those reported in bovine ovaries during the estrous cycle. The follicle size varied from 0.5 to 1.0

cm. and the corpora lutea were about 1 cm. in diameter. "Silent" heat or ovulation without estrus occurs frequently at the beginning and after the end of the breeding season. The estrual cycles tend to be longer or shorter in duration than the average at the beginning or end of the breeding season. Short cycles are more frequent in older ewes. Cycle length does not affect fertility.¹⁶² There was no tendency for individual ewes to have an early or late onset of the breeding season, so selection on this basis is not possible.

Sexual activity and signs in ewes, as in the mare, are nearly lacking in the absence of the male.^{2,3,67,78} Proestrus is rather indefinite and the onset of estrus is abrupt. Cessation of estrus is gradual. The symptoms of estrus in the ewe include restlessness, seeking out the ram, frequent switching of the tail as if the vulva itched, teasing the ram and standing immobile to be mounted and bred. In estrus the Dorset ewe has a characteristic stance. During an average heat period a ewe penned with a ram was teased 18 times, mounted 25 times and mated 6 times.^{77,78} Anorexia and swelling of the vulva are usual symptoms of estrus in the ewe. Most owners allow the ram to run with the ewes during the breeding season. Painting the brisket of the rams or having them wear a harness containing a marking device, in which various colors can be placed, is a common practice. Thus by observation of the rumps of the ewes, service can be noted and the date recorded. After 17 to 20 days a different color may be used to determine which ewes return to estrus. If many return, the fertility of the ram is probably questionable. Vasectomized rams can be used as teasers and "heat detectors" for ewes that are to be bred artificially. Administration of 50 to 100 mg. of testosterone propionate every other day for 20 days and then every 10 days or using testosterone implants resulted in producing normal male sexual behavior in treated ewes and others that could be used for estrus detection.^{28,97,132a} Rams can be operated upon similarly to bulls, to produce a lateral deviation of the penis at the time of erection. These surgically prepared rams were satisfactory as estrus detectors in ewes and semen could be collected from them.⁶

The ewe secretes mucus from the cervical glands but not in large amounts like the cow. Smearing the estrous mucus on a slide and allowing it to dry results in a fern or arborization pattern, similar to that in the cow, due to the high salt content in the mucus of estrus.³¹ The vaginal smear in the ewe is of limited diagnostic value in determining the stages of the estrous cycle.³ As in the cow, increased activity of the uterine muscle and edema of the endometrium occur during proestrus and estrus. The endometrium in some ewes may be black due to the

presence of melanoblastic pigment. This is not associated with stages of the cycle. The cervix is somewhat dilated and relaxed during estrus. Often ewes may attract rams by the odor of the vaginal mucus before the ewe is ready to accept coitus.¹ Ewes may occasionally show estrus during pregnancy. Eleven of 50 pregnant ewes had 1 to 3 "heats" during pregnancy.¹⁶²

The time of mating or artificial insemination during estrus in sheep is not as critical as in other animals.¹ The optimum time to breed is about 12 to 18 hours after the onset of estrus. Ovulation is spontaneous and usually occurs from 18 to 24 hours after the onset of estrus or from 12 to 24 hours before the end of estrus. In rare cases ovulation may occur after the end of estrus. In twin ovulation several hours or more may separate the time of ovulation of each follicle. Usually 1 to 3 ovulations take place and the rest of the follicles become atretic.

Ovulation Rate—Placing ewes on a high plane of nutrition or flushing for 2 weeks before mating increased the lamb crop by about 20 percent and flushing ewes for 3 to 5 weeks increased the rate of twinning to 40 percent or higher, compared to a 4 to 6 percent twinning rate in control, non-flushed ewes. Increasing the length of time of flushing beyond 4 to 5 weeks did not give a further ovulatory response.^{49,123,124} Breeding ewes fed a high plane of nutrition for 6 to 8 months before flushing resulted in a higher rate of twin ovulation than ewes fed a low plane of nutrition before flushing.⁵³ The lamb crop of range ewes was increased from 80 to 135 percent for a 6-year period by continuously feeding on a high plane of nutrition.¹⁰⁴ There is no evidence that high condition predisposes the ewe to sterility. Ewes on a high nutritional level had a higher ovulation rate, possibly a higher fertilization rate, and a slightly lower embryonic survival rate than ewes on a low nutritional level.⁴⁹ It was suggested that higher feeding levels caused an elevated plasma glucose, greater hypothalamic stimulation and release of larger amounts of gonadotropin causing greater ovarian activity and twin ovulations.^{76,103} The evidence that a high plane of energy intake was detrimental to embryo survival in the weeks following conception was not observed in ewes as in sows.^{53,123,124} In flushing ewes a high energy or TDN intake is needed; an increased intake of protein is not necessary.¹⁰³ The lambs, especially twins, of the ewes on a high plane of nutrition, were heavier, larger and stronger.^{123,124} When ewes had a severe diet restriction during the period from weaning to breeding, about a 4 month dry period, lambing percent was 22 percent lower the first year and 52 percent lower the second year than in control ewes even when a 20 day flushing period preceded the breeding season.¹⁵ Sim-

ilarly thin ewes affected with a chronic debilitating condition such as progressive pneumonia or visceral caseous lymphadenitis had a reduced reproductive efficiency when compared with normal ewes. The fertility and percentage of lambs born alive was 76 vs. 91–93 percent and 61 vs. 86 percent, respectively.⁶⁰

Other factors also influence the ovulation rate and the subsequent lamb crop. Ewe lambs, yearlings and young ewes as well as old ewes produce fewer twins and have lower lamb liveability.¹⁵⁵ The peak percent of lambs weaned was in 4-year-old ewes, range 3 to 6 years. However, a higher percentage of single lambs are viable at birth and are weaned than are twins or triplets.^{3,137} Crossbred ewes produced 9 to 23 percent larger lamb crop than purebred ewes when bred as ewe lambs. Older crossbred ewes produced 10 to 16 percent larger lamb crops.^{134,135} Ovulation rates are higher in the early to middle portions of the breeding season and decline later in the season.^{3,6} When ewes were given a 10 hour daily light period for 9 weeks starting late in the anestrus or transition period ovulation rates and lambs born per ewe increased about 25 percent from 1.2 to 1.65 lambs/ewe.³⁶ Certain ewes tend to have higher ovulation rates than other ewes. Thus selection of ewes born as twins or greater multiples from young mothers, large sheep of certain breeds, and those with open faces, free of wool, can be used to increase the lambing rate to 150 percent or greater in a flock.³ The mature ewes of the Finnish Landrace and Romanov breeds or their crosses frequently produce triplet or greater numbers of lambs.^{134,155}

Ovulation rates in Merino, Scottish Blackface and Finnish Landrace was 1.09, 1.36 and 3.37, respectively.¹⁵⁵ The breeding season midpoints for these three breeds were November 25th, December 20th and January 23rd, respectively and the incidence of "silent" ovulation for the three breeds was 35.6 percent, 16.2 percent and 7.3 percent. This strongly emphasizes the genetic differences between widely different breeds of sheep studied at one location.

Ovulations were slightly more frequent on the right ovary of ewes than on the left, 53 to 55 percent and 44 to 47 percent, respectively.^{24,80} In single ovulations 62 percent were on the right ovary. Twenty-six to 32 percent of embryos migrated from one horn to the other when twin ovulations occurred on one ovary; while only 0 to 10 percent migration occurred when a single ovulation occurred from one ovary.²⁴ As in cattle, an increased embryonic loss occurred in twin ovulations especially with twin ovulations from one ovary.

The LH content of the anterior pituitary gland started to be discharged at the onset of estrus and was completed 6 hours later when 52 percent of the LH in the

pituitary gland had been released.¹²⁹ The plasma surge in estradiol from maturing Graafian follicles stimulated by FSH preceded the LH release or surge. Small amounts of estrogen injected into sheep stimulated LH release.¹²⁹ A recent review of ovulation reported the maturing Graafian follicle is about 0.5 cm. in diameter and the plasma progesterone level is below 0.2 ng/ml. 1 to 2 days before estrus. The estradiol produced by the follicle reaches a peak of 15 pg/ml. in the peripheral plasma 24 hours before the onset of behavioral estrus that induces the release of GnRH and LH surge about 4 to 6 hours after the onset of estrus. The ovulatory follicle enlarges rapidly to about 1 cm. in diameter at the time of ovulation.¹²⁸

Gonadotropin levels in the anterior pituitary gland were high and constant during the nonbreeding season as were the presence of small follicles on the ovaries.^{1,88} Thus the onset of the estrous cycle in the late summer months associated with declining daylight may be triggered by a greater release of FSH and/or LH associated with an increased estrogen production. The ewe's pituitary gland is about 10 times as potent as the cow's in LH content and 5 times as potent in FSH content.¹

In the ewe progesterone is needed as well as estrogen to produce psychic estrus.² This probably accounts for some silent heats accompanying ovulations at the outset of the breeding season. Sixty-four ug. of estradiol was necessary to induce psychic estrus in ovariectomized ewes; if the injection was preceded by progesterone administration only 20 to 25 ug. of estradiol was needed to produce psychic estrus.¹ During the estrous cycle 10 to 15 mg. of progesterone in oil daily inhibited estrus. After ovulation, progesterone levels in blood plasma increased from 22.2 ng/ml. to 37.6 ng. by 9 or 10 days of the cycle and then decreased to 21.8 ng/ml. about 13 to 15 days after estrus or 2 to 3 days before the next estrus.¹¹⁹ The highest rate of estrogen excretion in the urine occurred at estrus with the lowest rate of excretion two days after estrus. No estrogens were found in the urine in sheep in the anestrus season. The principal estrogen excreted was estrone but some estradiol was also present in the urine.¹¹⁸ If conception occurred the level of progesterone in the peripheral plasma generally rose from 2 to 4 ng/ml. the first few weeks of gestation until day 60. After day 60 progesterone levels rose to 12 to 20 ng/ml. by day 110 due to increased progesterone production by the conceptus.¹²⁸ Ovariectomy after 55 days of gestation in the ewe is not generally followed by abortion because progesterone is produced by the placenta.

Following copulation and ejaculation of sperm into the vagina of the ewe, **sperm cell transport** is very rapid with spermatozoa appearing in the uterine tube within

15 minutes. Dead spermatozoa were also transported at a similar rate. Although about 800 million spermatozoa are in an ejaculate of a ram, some hours after copulation less than 100,000 sperm cells were in the uterus and several thousand or less were in the uterine tube. Spermatozoa retain viability and fertility for about 24 hours in the genital tract of the ewe.² The capacitation time for spermatozoa in ewes was 1.5 hours. Fertilization occurs in the uterine tube with sperm penetration of the ovum beginning about 3 hours after ovulation, pronuclei formed about 3 to 9 hours after ovulation, and the first cleavage of the ovum occurred about 20 to 30 hours after ovulation in the ewe.² The fertilized ovum enters the ovine uterus 3 to 4 days after ovulation.^{79,80} The low rate, 9 to 10 percent, of embryo migration from one horn to the other after single ovulations and the high rate, up to 60 percent or greater, after double ovulations has been discussed previously.²⁵

As in cows, estrogens injected into ewes cause a regression of the corpus luteum.^{14,64} Exogenous gonadotropins (HCG or LH) protected the C.L. of the ewe from regressing after an injection of exogenous estradiol. Developing follicles play a role in the regression of the C.L. in ewes.⁶³ Small doses of estradiol, 39 to 150 ug, given to ewes immediately before mating did not adversely affect sperm transport, ovum fertilization or embryo survival.⁷² Large doses of estradiol may hasten or delay ova transport and prevent conception.

Because ewes experience about 20 percent early embryonic deaths, especially those mated early in the breeding season, 0.4 mg per lb. of body weight of progesterone in oil was given daily subcutaneously to ewes for varying periods after breeding. This had no beneficial or harmful effects on fertility or embryonic deaths. Injections day 1 through 5 did tend to cause smaller C.L., but all ewes carried normal embryos.¹⁶⁷ Ovulation could be induced experimentally in both the luteal and follicular stages of the estrous cycle of ewes but ova produced during the luteal phase had a very low rate of fertilization.¹¹⁰ When natural C.L. were removed by laparotomy on day 5, 9 or 13, ewes came into estrus at 2 to 3.5 days after removal.^{86,87}

Transportation stress induced follicular growth and ovulation in anestrus ewes but since no declining C.L. were present no estrus was exhibited.^{152a} When hydrocortisone acetate was given to ovariectomized sheep, a marked increase in FSH occurred. In intact goats hydrocortisone stimulated the growth of luteal phase follicles and reduced the size and progesterone concentration of corpora lutea. The effect of hydrocortisone on inducing parturition in late pregnancy in ewes, cows and rabbits has been discussed previously. Parturitions in sheep late

in gestation were induced within 48 hours by the injection of 10 to 20 mg of dexamethasone.²

Utero-ovarian relationships in the ewe are similar to those observed in cows. Hysterectomy from early to mid-cycle in the ewe results in the maintenance or persistence of the C.L. for about 150 days or for the approximate length of gestation.^{64b,86,136} Unilateral hysterectomy regularly prolonged the life span of the C.L. about 17 days on the adjacent or ipsilateral ovary, but had no effect on the opposite or contralateral ovary. In one ewe with a C.L. on each ovary, unilateral hysterectomy prolonged the life of the ipsilateral C.L., while normal regression of the C.L. on the opposite ovary occurred. As in the cow the regression of the C.L. in a nonpregnant intact ewe is caused by prostaglandin released from the endometrium after the middle of the estrous cycle. The presence of an embryo in the uterus at 13 days of the cycle prevents the normal involution of the C.L. and the initiation of another estrous cycle by inhibiting the release or formation of prostaglandin and allowing pregnancy to proceed.¹³⁶ A single embryo in one horn can maintain a C.L. in both ovaries in intact ewes because the blastocyst extends into both horns.⁶⁷ Removal of the hypophysis of the pregnant ewe on day 30 of gestation caused abortion due to luteal regression because of the removal of the source of luteotrophin or prolactin.¹³⁶ If the hypophysis is removed from a pregnant ewe after day 60 of gestation, no abortion occurs because progesterone and possibly a luteotrophin are secreted by the placenta.

The presence of intrauterine plastic spirals or coils, an intrauterine device or I.U.D. causes a variety of effects in ewes that are somewhat similar to cows. A plastic coil in one horn of the ovine uterus inhibits sperm cell transport into the uterine tube and fertilization on both sides of the reproductive tract, and promotes spermicidal conditions in the uterine lumen.⁷⁰ The presence of an I.U.D. in the ewe's uterus caused more than 75 percent of the uterine contractions to be propagated toward the cervix; while in control ewes over 60 percent of contractions were propagated toward the uterine tube.⁹⁶

An I.U.D. introduced into a ewe's uterus within the first 3 days after estrus would prevent the normal development of the C.L. and hasten its regression and shorten the estrous cycle.⁶² If the I.U.D. was inserted on the 8th day of the cycle, the cycle length was normal or slightly prolonged.^{62,156} In I.U.D.-treated ewes about 25 percent of the ovulations were quiet or silent apparently due to a lack of enough progesterone from the regressing C.L. to cause the normal manifestations of estrus.⁶² When a uterine infection was produced by injecting *E. coli* into a ligated horn with an adjacent C.L. on day 3, C.L. growth was suppressed and early regression of the C.L. and a

shortened cycle occurred; infection at day 11 of the cycle caused a prolonged cycle. Thus infection acted in a manner similar to an I.U.D.¹⁸

Synchronization of estrus in ewes during the breeding season is possible using prostaglandins and long term suppression of estrus, 12 to 16 days, with progestogens alone, usually as vaginal pessaries impregnated with 60 mg. MAP or 30 to 40 mg. of flugestone (**Cronolone**), or combined with 500 I.U. PMSG on the day the pessary is removed as in anestrus ewes.^{87,91b,93b} A variety of treatments utilizing the prostaglandins have been proposed.¹⁴⁴ Ewes are observed carefully for estrus for 5 days since prostaglandin is ineffective if given before 4 days after estrus. Those not in estrus during this period are given 5 to 15 mg. P.G.F._{2a} or 100 to 125 ug. cloprostenol and usually 50 to 80 percent of the ewes will show estrus in 2 to 5 days after the injection and accept service by the buck for a period of 31 to 52 hours. Ovulation rates are normal. If random injection of the flock is used then all the does are given prostaglandin and the second dose is given 9 to 11 days later with up to 90 percent or more of the flock coming into estrus within 1-1/2 to 5 days. Giving 500 IU PMSG 2 days before the second dose of prostaglandin induces an earlier onset of estrus.¹⁴⁴ Although the evidence is somewhat contradictory, there is a lower fertility or conception rate, seldom exceeding 56 percent, on breeding the first estrus after the use of prostaglandins. This is apparently due to inhibition of spermatozoal transport in the cervix and uterus due to loss of motility and death of sperm similar to the effects of the persistence of a level of progesterone.^{72a,73} This reduction in fertility is variable and apparently not as noticeable as that following long term injectable progesterone therapy to synchronize ovine estrus. A recent study of double injection of P.G.F._{2a} at a 10 mg. dose at an 11 day interval in ewes in the breeding season compared to MAP vaginal sponges for 8 days with 10 mg. P.G.F._{2a} given at the time of withdrawal of the sponge resulted in 82 to 93 percent of the ewes showing estrus in 1-1/2 to 5 days, (1-1/2 to 3-1/2 days for the latter group) and a 60 to 80 percent conception rate, average 71.7 percent, after AI service 12 and 24 hours after the onset of estrus.⁹⁴ Worldwide the vaginal pessaries or sponges and PMSG are most preferred for estrus synchronization in cycling and anestrus ewes.⁸⁷

Synchronization of estrus in anestrus ewes has received much study over the past 20 years. Results of studies utilizing progestogens given orally, intramuscularly, intravaginally or subcutaneously as implants alone or combined with PMSG up to 1971 have been reviewed.¹²⁷ Although many of these studies were encouraging, at present approval by the Federal officials

for use of progestogens has not been forthcoming. PMSG in a standardized form is not readily available in the U.S. The estrogens have been proven to be of no value for synchronizing or inducing estrus in ewes. Fertility of ewes following the use of long-term progestogen therapy is reduced at the first estrous period due to poor sperm transport in the ewes' genital tract.^{73,128} Use of vaginal pessaries containing progesterone have shown the most promise because the exogenous source of progesterone can be rapidly removed allowing the prompt development of the estrous cycle. However problems of vaginitis, adhesion of the pessary to the vaginal wall and loss of pessaries have complicated this procedure. Prostaglandins are ineffective during the anestrus period because functional corpora lutea are not present. All of the above chemical procedures for estrus synchronization were most effective during the transitional period between the anestrus period and early in the normal breeding season. Synchronization of estrus or establishing the estrous cycle in the anestrus period of late spring and early summer has been less successful and impractical because of a great variation in response and results.

Furthermore inducing estrus in ewes out of the regular breeding season creates additional problems with rams as at this time libido and production of spermatozoa are at a low level.¹²⁸ This can be alleviated to some extent by maintaining and introducing a large number of rams. Artificial insemination of ewes is costly because of the time and labor involved in estrus detection, inseminating at the correct stage of estrus, and the collection and extension of fresh ram semen. Frozen ram semen has a reduced survival time in the ewe's genital tract so timing of insemination is important. It is usually recommended that ewes be serviced 12 to 14 hours after estrus is first observed or 48 to 55 hours after progestogen withdrawal in synchronized ewes.¹²⁸

Ewes synchronized during the anestrus season and the breeding season with progestins and PMSG had an increased ovulation rate but had markedly higher reproductive losses, 58 and 49 percent respectively, compared to untreated ewes bred during the breeding season, 25 percent.⁹⁵ These losses were due to both increased fertilization failure and increased embryonic mortality. The increased fertilization failure was due to both decreased tubal numbers of spermatozoa and a decrease in number of accessory spermatozoa/ovum possibly related to poorer out-of-season semen quality and abnormal sperm transport.⁷³ The increased embryonic mortality in treated ewes was associated with an increased variation in stage of embryo development within the ewes indicating asynchronies of timing of onset of estrus, ovulation and fertilization.⁹⁵ The use of artificial insemination with fresh

semen produced better conception rates than the much lower conception rates with frozen semen.⁵⁸ Further studies on estrus synchronization and induction during the anestrus season are continuing. (See ewe productivity at the end of this chapter.)

Pathological Changes in the Reproductive System of the Ewe

Anatomic defects of the genital tract of female sheep are uncommon. Intersexes may occasionally be observed in sheep. Freemartins, such as occur in twin births in cattle, are rare in sheep.⁹³ Since other anatomic defects or arrests in development such as uterus unicornis, uterus didelphys, persistence of the median wall of the Mullerian duct with a fleshy pillar caudal to the cervix, other arrests in development of the Mullerian duct, and persistence of the hymen occur in other species, they probably occur in sheep but are rarely recorded. Undoubtedly they are highly unusual. One ewe was reported with a bifurcation of the cranial part of the vagina.³⁸

Pathological lesions or diseases of the reproductive system in sheep and goats are similar in most respects to those in cattle. Vulvitis, vaginitis, cervicitis, metritis, pyometra, perimetritis, and salpingitis may occur in sheep usually as sequelae to dystocia, difficult parturition, retained placenta, and delayed involution of the uterus.⁹³ These acute or chronic infections in the ewe are handled in a manner similar to the treatment for these infections in cattle. In retained placenta, which is much less common in ewes than cattle, the uterus may be treated locally, preferably with a broad-range antibiotic, and the placenta is allowed to drop away. For a valuable ewe a



Figure 151. Parovarian Cysts Adjacent to the Left Ovary in a Ewe. (Courtesy K. McEntee.)

better treatment is to give parenteral antibiotics for 3 to 5 days and not to place any drug in the uterus or to attempt to remove the afterbirth. Manual removal of a retained placenta is not indicated due to the small size of the genital tract.

A group of 25 ewes that had failed to breed for two consecutive seasons were mated a third season.¹¹¹ Eleven ewes lambled after only one service. Five ewes were bred and apparently conceived, but on postmortem examination showed evidence of interruption of pregnancy before term, and 8 ewes were bred at several estrous periods but failed to conceive. On postmortem examination 6 of these sterile ewes were found to have occluded or cystic uterine tubes and one ewe had a mummified fetus. An incidence of 8.7 percent of abnormalities in the reproductive tracts of 276 ewes was described.⁹³ These included parovarian cysts, hydrosalpinx, bursal adhesions, and adhesions of the uterus to the abdominal viscera. These lesions apparently account for only a small percentage of the infertility in ewes.⁴⁶ Extensive and severe changes could be produced in the genital tract in the ewe by feeding chlorinated naphthalenes.⁹⁹ These changes were characterized by an enlarged uterine horn and cervix due to marked squamous metaplasia with profuse keratinization of the endometrial glands as well as keratinization and ulceration of the vulva. Naturally-occurring cases of hyperkeratosis or X disease have not been seen in sheep.

Tumors of the ovaries and genital tract of the ewe are rare. Several leiomyomas affecting the uterus of sheep have been recorded.⁵⁰ Rare granulosa cell tumors of the ovaries and leiomyomas of the uterus of sheep have also been reported.^{27,109} An adenoma of the pituitary gland of a ewe has been observed.²⁷ Rare cases of lymphosarcoma or reticulum-cell sarcoma, myeloma and squamous cell carcinoma of the vulva of ewes have been described.¹⁰⁶

Infections of the genital tract other than postpartum infections apparently are seldom a cause for infertility in ewes. This may be explained in part by the long period between breeding seasons, in which recovery can take place. Vibriosis and brucellosis, the latter usually due to *Br. melitensis* or *Br. abortus* are characterized by abortion. Infertility in ewes associated with vibriosis and brucellosis has not been described. The incidence of embryonic deaths in ewes bred early in the breeding season was about 20 percent. There was no indication of an infection associated with the condition.^{38,41} In observing and examining rams with various degrees of infertility, an enzootic venereal type of infertility spread by the ram to the ewe, as is observed in cattle has not been reported.^{66b,160} The infectious causes of abortion, such as

listeria, rickettsial agents, and others have not been associated with infertility.

Ulcerative dermatosis, lip and leg ulceration or ulcerative venereal disease due to a virus can be spread by an infected ram or buck to a susceptible ewe or doe through breaks in the skin, causing a necrotic, swollen, bleeding lesion on the cutaneous and mucous surfaces of the vulvar lips.^{4a,4b,13,146,147} The lesion usually starts at the inferior commissure of the vulva and spreads upward. Only rarely is the vagina involved. The lesion is an ulcer covered by a scab. Removal of the scab reveals a shallow, bleeding crater containing a small amount of creamy pus. The disease is usually spread to the ewe at the time of coitus by an infected ram that has similar lesion on its penis and sheath. Occasionally the disease may spread to wethers and to ewes that have not been bred.^{4b} This venereal disease of the external genitals should not be confused with contagious ecthyma which is due to a different virus and the lesions are proliferative. In a recent report it was indicated that the viral agents causing these two diseases might be related since there was cross neutralization between the two viruses in serologic studies.¹⁴⁵ The symptoms of ulcerative dermatosis usually subside within a week or 10 days. No successful specific treatment is available. Five percent copper sulphate has been advised for use in treating these lesions but should only be applied externally. No vaccine is available. Rams with lesions on the prepuce causing posthitis should not be purchased or placed with ewes during the breeding season. This disease, although a cause for cessation of breeding until the lesions are healed, is not characterized by infertility. However in the acute phase the ewe may refuse to copulate due to irritation and pain.

Ureaplasma have been isolated from the genital tracts of ewes with granular vulvitis³⁴ and from the uterus of a few ewes that apparently suffered early fetal losses.^{92b} A recent report indicated that in sheep, ureaplasmosis appears to be a venereal disease possibly capable of causing infertility, low birth weight of fetuses,^{92a} and acute vulvitis.^{6b} The significance of infertility from this common organism in the genital tract of ewes and cows must be further evaluated.

Mules' operation has been described^{108,166} for the **prevention of blowfly strike** (myiasis) caused by folds of skin on either side and below the vulva becoming moist with urine or soft fecal material resulting in an inflammation, bacterial growth, and an odor that attracts the blow flies to lay their eggs in the site. The moist fleece provides the hatching maggots with food, warmth and protection. Since clipping the wool in the area or applying insecticides to prevent blowfly strike are short-lived practices, Mules' operation has been used extensively in

Australia to increase the area of smooth skin around the vulva and anus in Merino or other heavily-fleeced breeds. Also, the tail should be docked short so that no long wool lies against the vulva. Mules' operation is performed on recently clipped sheep during the cold season in the spring or fall when there are no flies. The folds of skin ventral and lateral to the vulva are removed and healing is allowed to occur without suturing.¹⁶⁶ The resulting healing and scarring eliminates the skin folds and long wool lateral and ventral to the vulva and prevents blowfly strike.

A vulvitis that occurred in ewes on clover pasture similar to the noncontagious posthitis that was seen in wethers on lush clover pasture has been described in Australia.¹³⁸ There was no evidence that estrogens in the clover were a factor in this disease. The ulceration, scabbing and scarring of the ventral commissure of the vulva in this disease led to its disfigurement or loss with a resulting soiling of the rear parts with urine predisposing to flystrike even in ewes on which Mules' operation had been performed.

Nutritional deficiencies in sheep and their effect on fertility have been extensively studied. The same general nutritive deficiencies affecting reproduction and fertility in cattle also affect sheep. Most deficiency diseases affecting reproduction in ewes on range are multiple and involve a lack of protein, and a lack of vitamin A. The effects of inanition on fertility are more pronounced in immature than in adult animals and they are characterized by failure of estrum and delayed puberty. A low plane of nutrition in ewes resulted in subestrus with undetected estrus, with cycles 26 to 42 days in length.⁸⁵

A low protein diet is to be avoided if a high percentage of lambs is to be produced.¹⁰⁴ The symptoms of vitamin A deficiency are similar in the ewe and cow.^{74,123,124} Pregnancy in vitamin A deficient ewes usually terminates in abortion or the birth of dead or weak young. The female is more susceptible to vitamin A deficiency than is the male. The estrous cycle, ovulation, and early fetal development are not noticeably affected in sheep even when partial night blindness due to Vitamin A deficiency is exhibited.^{123,124} In drouth years feed low in vitamin A is often also low in energy, protein, and phosphorus. Vitamins E, C, B complex, and D are not necessary for reproduction in the ewe. It is possible, however, that a lack of cobalt, an essential part of vitamin B₁₂ would cause a deficiency of rumen bacteria, and anorexia with secondary inanition. Severe deficiencies of cobalt may result in debility, failure of estrum, and the birth of weak lambs. Estrum in ewes was regular on a cobalt-deficient diet but only 48 percent of the lambs born to cobalt-deficient ewes were strong, as compared

to 92 percent of the lambs from ewes fed a cobalt supplement.¹⁶ Postnatal losses of lambs from ewes fed low levels of cobalt were 58 percent as compared to 17 percent for the lambs nursing the ewes receiving cobalt in their diet. Copper deficiency in sheep characterized by infertility and irregular estrous periods has been reported in certain areas of South Africa.

Reproduction is not affected by a low phosphorus diet until the usual symptoms of phosphorus deficiency develop.^{123,124} Symptoms of phosphorus deficiency in sheep are the same as in cattle. A low protein diet was not as severe as one low in both protein and phosphorus.¹⁰⁴ The reproductive symptoms of a phosphorus deficiency, which is usually complicated by low protein and vitamin A level, are: delay in onset of puberty and estrum, irregular estrous periods, and a tendency to produce only one lamb every two years. Abortions are uncommon but weak or dead young may be expelled at term. Impaired fertility is unlikely when the ewe or doe is receiving protein supplements or minerals containing phosphorus. Other trace mineral elements such as iron and iodine may also be lacking. In several mineral and protein deficiencies, ewes may pull and eat the wool of other ewes in the flock.

Ewes but not rams, require Vitamin E and selenium to have satisfactory reproduction.^{20,35,69} Not only could selenium deficiency in ewes in New Zealand cause neonatal death losses due to several myocardial lesions but in selenium deficient areas, farms would experience an incidence of 10 to 30 percent barren or open ewes after service and apparent conception.⁶⁹ Giving ewes 5 mg. of selenium monthly during pregnancy or 25 mg. in one dose after mating reduced the number of barren or open ewes to 2 to 4 percent compared to 30 percent open ewes in the control or untreated ewes. Although evidence would indicate that a selenium deficiency occurred in New Zealand, it should be noted the diseases corrected by selenium therapy were referred to as "selenium responsive" diseases. It is possible that some other factor(s) may cause the primary or basic disease.

Ewes fed kale had a short duration of estrus of about 22 hours and a slight increase in embryonic deaths.¹⁶¹ Kale feeding also resulted in anemia and produced a goiterogenic effect.

In Australia a specific type of infertility in sheep due to pasturing on subterranean clover rich in estrogens is observed. In this condition, the incidence of sterility in ewes may be 30 percent or even greater.¹⁰ Dystocia due to uterine inertia may have accounted for 30 to 40 percent of the fetuses being expelled or removed dead and for the death of 15 to 20 percent of the ewes. Prolapse of the vagina was seen in approximately 10 to 12 percent of the ewes. The sterile ewes failed to conceive on re-

peated services and on postmortem examination of the genital tract a cystic degeneration of the endometrium was observed that varied in severity from microscopic to gross lesions. The estrous cycles were normal and cystic ovaries did not occur. The infertility persisted and was irreversible even when the affected ewes were changed to pastures free of the subterranean clover.^{132,150,151} Ovulation occurred regularly but fertilization or implantation were prevented by the pathologic "Swiss cheese" type of endometrium. In a recent study of 49 ewes with a permanent phytoestrogenic sterility it was demonstrated that only 57 percent of the affected ewes showed estrus accompanied by ovulation vs. 90.5 percent of the control ewes, and 21 percent of the ovulations in affected ewes were not accompanied by behavioral estrus vs. only 4 percent in control ewes.¹ Progesterone assays were normal in 7 of 12 affected ewes that had normal length estrous cycles. Four of 5 other ewes had prolonged estrous cycles of 21 to more than 23 days with prolonged high levels of progesterone. In 43 affected ewes with a C.L., the C.L. failed to regress in 5 of 7 ewes with hydrops uteri and 3 of 36 ewes without hydrops uteri. These abnormal life spans of C.L. in affected ewes were considered to be caused by endometrial changes in the uteri of affected ewes.¹

The "toxic" principle in the Dwalganup strain of subterranean clover was an isoflavone derivative, genistein or 5:7:4 trihydroxyisoflavone, that was one-fifth as potent as estrone in estrogenic activity.^{30,46} Genistein may be found in amounts of 100 mg. per 100 gm. of fresh subterranean clover. Reducing the amount of subterranean clover in a pasture by increasing the amount of grasses controlled the disease. Possibly since the pasture season coincides with the anestrus season in sheep, when the ewe is not cycling and progesterone is not produced, the ingested estrogens may cause more severe lesions and disease in sheep than in cattle which are generally not affected by the level of estrogen in the clover pastures. Ewes in Australia, grazing red clover pastures were similarly affected as ewes on subterranean clover pastures.^{9,149} Estrogens have also been found but in lower quantities in other legumes such as ladino clover and birdsfoot trefoil.^{11,120,131} Injection of 0.03 to 0.09 mg. of stilbestrol per ewe 3 days a week for 6 months to 2 years caused a high incidence of sterility, persistent and permanent cystic change in the endometrium.¹⁵¹ A few ewes with cystic endometritis developed pyometra in a manner resembling that seen in dogs. The estrous cycle remained normal. Cystic ovaries have not been described in ewes.

Fertilization Rates and Prenatal or Embryonic Death Rates in Ewes. In 80 pregnant ewes there were normal

fetuses equal to only 87 percent of the corpora lutea present. The numbers of atrophic fetuses and missing eggs were about equal.^{68a} The incidence of fetal death was estimated in a similar manner and it was reported that 16 percent of the corpora lutea were not accounted for by live fetuses but early embryonic death with complete resorption could not be detected.^{71b} Increased fetal deaths occurred with an increase in number of ova released, 8 percent with 1 ovum, 26 percent with 2, and 43 percent with 3 ova. This fetal mortality may be more apparent than actual when these figures are interpreted to indicate that with a large number of eggs more embryos must die before the pregnancy is terminated.^{22,23} Fertilization rates and embryonic death rates in Western ewes bred throughout the breeding season showed the overall embryonic death rate on the basis of 18-day nonreturns was 20 percent but that on the basis of the lambing rate the embryonic death rate was nearly 30 percent.^{22,23} A much higher embryonic death loss developed in ewes with 3 C.L. compared to ewes with 1 or 2 C.L.⁸⁰⁻⁸² A 20 to 24 percent loss of fertilized eggs is normal in the ewe.¹³⁰ A prenatal death loss in Merino sheep in Australia of about 25 to 30 percent from 3 weeks after conception to term was noted.^{107b} Ewes bred once early in the breeding season showed an embryonic death rate of 20 percent and a failure of fertilization in 38.9 percent of the ewes.^{38,41} Failure of fertilization was the most important factor accounting for the low lambing rate. Fifty-four of these ewes bred artificially with semen having a 20 to 50 percent spermatozoan motility rate had about a 31 percent conception rate, while 100 ewes bred with semen having a 60 percent or better motility rate had a 62 percent conception rate. The embryonic death rate in both groups was about equal. When rams from high and low prolificacy lines of breeding were used on unrelated ewes there was no difference in ovulation or fertilization rates. However pregnancy rates and lambing rates were higher in ewes bred to rams selected from the high prolificacy lines than rams from the low prolificacy lines.²¹

Ewes bred early, August 1 to September 15, had a fertilization failure of 64.3 percent, 16.7 percent due to defective ova and 47.6 percent due to poor sperm, with a conception rate of 25.5 percent.⁷⁷ In ewes bred from September 16 to October 25, the respective figures were 34.3 percent, 29 and 31.4 percent, and a conception rate of 59.2 percent. The deaths of the embryo were high early and late in the breeding season.⁵ In asynchronous heats and ovulation, the eggs failed to fertilize. The high figure of 40 percent early embryonic deaths by 24 days of gestation in 65 ewes was reported.⁵

High ambient temperatures, especially during and

shortly after estrus, have an adverse effect on fertilization and the survival of the zygote. Ewes exposed to an ambient temperature of 90° F on the 12th day of the cycle through estrus had a fertilization rate of 51.9 percent, as determined 3 days after breeding, compared to a 92.6 percent rate for control ewes kept in a cool environment.^{38,41} Only 3.7 percent of ova from the control ewes were grossly abnormal compared to 44.2 percent of the ova from the ewes kept at 90° F. Embryo loss based on fertilized ova that died was 91.7 percent compared to 4 percent loss in control ewes at 24 days after breeding. In sheared ewes there were 32 percent abnormal ova and the rise in body temperature was 1.8° F. In unsheared ewes there were 55.6 percent abnormal ova and the rise in average body temperature was 2.6° F. Ewes kept at an ambient temperature of 90° F for 24 hours during estrum had only a 10 percent lamb crop from service at that estrum. If the 90° F temperature was maintained for 24 hours at 3 or 5 days of gestation the lamb crop in each group of ewes was 35 and 40 percent. The control ewes produced an 85 percent lamb crop. The early ovum during the initial stage of cleavage is most sensitive to heat.⁴² This effect on the early zygote in ewes is similar to the effect of high ambient temperatures on cattle shortly after service (See Infertility in Cows) After reviewing the adverse effects of thermal stress in ewes on fertilization rates early embryonic death rates and lambing rates, one study⁷⁵ showed that maintaining ewes at high ambient temperatures, 36° C, resulting in a rise of 1.4° C in body temperature caused significant decreases in the incidence of behavioral estrus, the preovulatory L.H. surge and in the plasma progesterone level between days 7 and 13 of the cycle. These endocrine imbalances may contribute to the decreased reproductive efficiency of heat-stressed ewes.⁷⁵ Rams exposed to high ambient temperatures, especially with much wool on the scrotum also have greatly lowered semen quality due to degeneration of the seminiferous tubules. Another study^{3,4} confirmed the above effects of high ambient temperatures on the early ova by ova transfer. A recent study indicated that the greatest embryonic death loss in heat-stressed ewes conducted during early pregnancy occurred from days 10 to 23 of gestation.⁴² Thus 90° F ambient temperatures are harmful to fertilization and early embryo survival and may be a cause of seasonal infertility in ewes. Ewes to be bred early in the season should be kept sheared and cool. Possibly early breeding in the summer months should be avoided. Ewes that were heat-stressed during the last two-thirds of the gestation period when compared to ewes kept cool, had fewer lambs, 81 vs. 100 percent, the lambs were lighter and smaller and fewer lambs survived, 57 vs. 81 percent.¹³³ A high plane of feeding had no effect

on embryonic or fetal death rates. Ewes giving birth in a hot environment had a significantly shorter gestation period. This is interesting in the light of the influence of the glucocorticoids and stress on the initiation of parturition.

Ewe Productivity—Because ewes can produce twins or triplets and have a 145-day gestation period it should be feasible to produce 3 lamb crops in 2 years. This goal has been sought by many investigators and sheep farmers but currently a practical way to achieve it has not been formulated.¹²¹ It is recognized that if such a goal is to be reached management of the flock must be excellent. Some of the factors mitigating against such a goal is the photoperiodicity of the breeding season in sheep. Although excellent lamb crops can be obtained from fall and winter breeding seasons, the lamb crop from late spring breedings, whether produced by “chemical” or light manipulation methods has generally been low.^{43,153} Even with the best of control and management it is difficult to produce more than 2 lambs/ewe/year.^{91b} Of the “chemical” methods for inducing estrus and conception the prostaglandin and progestogen treatments alone can not be recommended. However, even the progestogen-PMSG controlled breeding is best in the fall breeding season.¹²¹ Progestogens and prostaglandins have not been approved by Federal agencies for use in ewes and PMSG is not readily available in the U.S. Yearling or younger ewes do not do well in controlled breeding regimens. Possibly certain breeds might be more suited to this intensified production scheme.

Currently the best or most easily accomplished practice to increase ewe productivity is to crossbreed using the Finnish Landrace on the standard breeds in the U.S.^{43,113} Half-bred Finn ewes gave birth to 42 percent more lambs and weaned 24 percent more kilograms of lambs than 1/4-Finns and 52 percent more lambs and 38 percent more kilograms of lamb than did Suffolk-Rambouillet cross ewes.¹¹³

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INFERTILITY IN DOES

Reproductive Physiology

Puberty—Depending upon breed, season of birth, latitude and level of nutrition, puberty usually occurs about 6 to 8 months of age in the Swiss breeds of goats in the temperate latitudes. Young bucks and does should be separated before 5 months of age. Certain pygmy does may reach puberty by 3 months of age.^{22,25} Does should not be bred until they reach 60 to 70 percent of their adult weight, about 80 to 90 pounds, to assure higher

conception rates and safer parturitions. Delaying breeding until they reach this weight often results in breeding does after they reach a year of age. Twin births are common in young well-grown primiparous does. In later parities twin or triplet births are more common and quadruplet births are not rare.

The estrous cycle—Does and bucks in northern temperate climates are photoperiodic with a breeding season extending from late summer (August) to early spring (February and March) with the peak of the breeding season in late fall (October) through early winter (December). During this breeding season brought on by shorter daylight hours, the does are polyestrous with most cycles being 20 to 21 days in length.^{22,25} In the tropical regions near the equator the breeding season is not dependent on photoperiods and extends throughout the year.^{13,25} Short cycles of 5 to 12 days in length are not uncommon in young does at puberty or older does at the beginning of the breeding season. Long cycles 40 to 50 days, at the end of the breeding season are also fairly common.^{6b,22,25} Further studies on the cause of these abnormal cycles are indicated. Estrus may occasionally, 1 to 5 percent, be observed during pregnancy.^{6b} Between early March through May, nonpregnant does in the temperate zones are anestrous. Between May and July is the transition period from anestrous to ovarian activity and cycling. Bucks like rams and stallions do not have a restricted breeding season as do females of those species. But during the breeding season bucks are sexually more active, have a stronger “buck odor,” and produce better quality semen. Like sheep and swine placing bucks in a group of does early in the breeding season often induces estrus in many of the does within 7 to 10 days,^{22,25} probably due to the release of GnRH or LH (see ewes).

The estrous period is variable in length depending on the interpretation of behavioral signs indicating the onset and termination of this period. It is generally given as 32 to 40 hours with ovulation occurring about 30 to 36 hours after the onset of estrus.^{19,22,25} In the Angora breed estrus is about 22 hours in duration.²² Another study²⁵ indicated proestrus lasts about 24 hours during which time the buck follows the doe but she will not stand for service. Once standing estrus occurs it only lasts 12 to 24 hours. When does are observed in estrus they should be bred then and again 12 hours later.^{13,26b}

Signs of estrus in does is detected by a teaser or breeding buck because does, like mares and ewes, rarely mount other females or stand to be mounted by other does as do cows.²⁵ If a rag is rubbed over an older buck's scent glands located caudomedially to his horns and stored in a tightly-covered jar, this “buck jar” is warmed, opened and presented daily to each doe in a small flock.²⁵ If the

doe is in estrus she will be very interested in the jar. In the presence of a buck a doe in estrus will stay close to him. Her external genitalia may be more swollen, reddened and moist during estrus. Rapid up and down or side to side movements of the doe's tail, flagging, is a good sign of heat along with restlessness, increased frequency of urination, increased bleating and decreased milk production and appetite. Vaginal smears are of limited value to identify the stage of the cycle.²⁵ As in other domestic species a speculum examination of the vagina and cervix will show an increased reddening of the mucosa, a variable amount of clear mucus in the cervix and on the floor of the vagina early in the estrogenic stage of the cycle. The mucus becomes more cloudy together with a more relaxed cervix in midestrus. Metestrous bleeding, as occurs in cows, is not present in does.²⁵ Sexual behavior in the buck usually consists of nuzzling the doe's perineum, pushing or butting her rear parts, flehmen and flicking out the tongue, striking out with a forefoot and emitting a low-pitched sound.^{26b} Mounting and copulation is rapid and quick.

As in sheep the introduction of bucks into a flock of does at the beginning of the breeding season produces a prompt stimulation of the onset of the estrous cycle. This effect is probably caused by the combined senses of sight, smell and contact. In one study 66 percent of the does kidded between the 8th and 12th day of the kidding season. This indicated that most does come into estrum about 10 days after the bucks were introduced.^{20,21,24a} Recent reports^{17,27} have demonstrated rather conclusively that introduction of bucks into flocks of does in the early breeding season or late anestrus season and observing and monitoring the latter with progesterone assays of blood plasma, that a synchrony of estrus was obtainable. Sixteen of 17 does were in estrus at an average of 5.5 ± 1.3 days after the bucks were introduced, with 31 of the does showing a subsequent progesterone profile, with concentrations of 3 to 4 ng/ml., characteristic of a normal diestrous period. When the bucks were introduced into the control does 15 of the 17 exhibited estrus within 7 ± 1.5 days. Short six-day estrous cycles were seen in 4 does but the progesterone concentrations between the estrous periods never rose above 1.0 ng/ml indicating the first period was anovulatory. Thus it appears that at the onset of the breeding season in goats the first estrus is usually clinically observable and ovulatory.²⁷ This is probably related to a small, brief but significant rise in plasma progesterone levels occurring just before this first estrus.⁴ Occasionally a short anovulatory cycle has been reported.²⁷ This general pattern in does of a standing estrus and ovulation at the first estrus of the breeding season apparently differs from that in ewes in which the

first estrus and ovulation is "silent" or without signs of estrus.

Following copulation and ejaculation of sperm into the vagina of the doe, sperm cell transport is very rapid with spermatozoa appearing in the uterine tubes within minutes with fertilization occurring in the ampullae of the uterine tubes. Does usually ovulate 2 ova with 3 being quite common. So they are generally more prolific than most breeds of sheep or cattle.¹⁹ After ovulation it normally requires about 4 days for the fertilized ova or embryo to reach the uterus. As with ewes, the plane of nutrition, degree of growth and development, and freedom from disease influences the ovulation rate.²²

The corpus luteum in the doe persists throughout pregnancy as in the cow. Thus ovariectomy at any time during pregnancy will result in abortion unless progesterone replacement is instituted. The conceptus, placenta and fetus, does not produce sufficient progesterone like they do in ewes, to maintain pregnancy in the absence of the CL in the middle or latter half of gestation.¹⁹ Twice daily doses of 50 units of oxytocin given to does on days 3 to 6 of the estrous cycle shortened the cycle to 6 to 7 days. The next cycle was normal in length. This oxytocin stimulated uterine prostaglandin F_{2a} release in does to cause luteolysis in the same manner as occurs in cows given oxytocin several days after estrus to cause failure of normal CL development.

Synchronization of estrus in the doe has been studied outside the breeding season (during the anestrus period) and during the breeding season. In the former period plasma progesterone levels are very low, below 1 ng/ml. and there is little or no ovarian activity. Thus prostaglandins are ineffective during this anestrus period. PMSG at doses of 400 to 750 IU, depending on the season, month of lactation and lactation rate, given intramuscularly, or combined with HCG, have been reported to induce estrus in 2 to 3 days with about 40 to 50 percent conceptions.^{6b,13,25} Progesterone impregnated vaginal pessaries have been inserted for 17 to 21 days with PMSG given 48 hours before removal. By using large numbers of spermatozoa by artificial insemination, this procedure has been reported to be highly successful. The use of 100 ug GnRH daily for 4 or 5 days may produce estrus.²⁵ During the transition period between anestrus and the breeding season synchronization is promoted, as mentioned previously by the introduction of bucks into the herd. Manipulation of the photoperiod to advance the breeding season by keeping both does and bucks under daylight or artificial light for 14 to 18 hours a day for 3 months or 19 hours a day for 70 days in midwinter and then reducing the amount of daylight to 6 to 10 hours per day in the spring.^{4,25} This will usually successfully

synchronize the herd and result in conception in over 50 percent of the does.

A practical procedure to alter the photoperiod and breeding season of does so that a uniform supply of milk could be maintained throughout the year was described.³ Since most does under natural conditions freshen from January through May in the northern hemisphere, September through November freshenings are desired. To accomplish this 40 watt fluorescent bulbs, 1 foot (12 inches) of bulb for 10.5 square feet of floor space, 9 feet above the floor were turned on by a timer for twenty hour days starting on January 1. The lights were turned off from 1 to 5 am. Continuous 24 hour lighting did not produce the desired results. From one hour after sunrise to one hour before sunset the barn light may be turned off to save energy. This regimen was continued for 60 days for both does and bucks or until between March 1 and 15. At this time normal daylight of 14 to 15 hours exists and this shortened day length initiates estrus cycling 7 to 10 weeks later or late in April or May and cycling continues into June with 80 to 90 percent conceptions during that period. Putting yearling does and bucks on a 19 hr./day-light regimen for 70 days starting in January and then introducing the bucks to the flock 42 days after the 70 day light period resulted in 79 percent of the does coming into estrus and ovulating within 21 to 30 days.⁴ Sixty three percent of all the does or 80 percent of the does ovulating conceived at this estrus. Thus the breeding season was advanced to 60 to 80 days and a degree of synchronization achieved without hormones.

Breeding bucks need to be light-stimulated like does or their libido may be poor. If bucks are to be used in both breeding seasons their feeding and management should be excellent.³ Standing heat in light-treated does is shorter, often only 8 to 10 hours, during the artificially established breeding season and often occurs during the night hours so clinical signs of estrus are often not observed. Therefore handmating of all does is not possible and opportunity for pen mating is necessary. When the latter practice is used the attendant should check the does every other day for the discharge that mats the tail following service. Often a pen of light-treated does may come into estrus at the same time. To obtain maximal milk production during November and December 16 hours of daylight should be provided by the supplemental use of lights. If the above regimen for light stimulation during January and February is provided the entire herd, it has no effect on does or bucks not bred until the natural fall breeding season.³

During the breeding season synchronization is best achieved by the injection of 1.25 to 2.5 mg. of prosta-

glandin F_{2a} or its equivalent of prostaglandin analogue, 125 to 150 ug. of cloprostenol, to produce luteolysis or involution of the CL.^{5,13,25} If estrous cycling is occurring a single dose should result in estrus within 2 to 3 days in about 60 percent or more of the does. Another method is to inject PGF_{2a} in 2 doses four hours apart. In cycling does PGF_{2a} was luteolytic as early as day 5 of the cycle and does were in estrus 50 to 57 hours after the second injection with a preovulatory peak of LH observed at 55 hours after injection.¹⁸ Similar posttreatment results were observed with 2 treatments, 11 days apart and 100 percent of 20 does were synchronized compared to 85 percent with a single treatment.¹⁶ The estrous period was normal and 30 of 32 does, 93 percent, conceived by natural service. Although doses of 5 to 15 mg of PGF_{2a} were originally recommended to produce luteolysis in does, smaller doses of 1.25 to 2.5 mg, were found to be equally as effective.⁵

Another procedure for synchronizing estrus in does during the breeding season is administering progestogens to suppress estrus and cycling in does for 20 to 22 days^{6b} alone or usually with 300 to 700 IU PMSG at the time of progestogen withdrawal. Progestogens may be given either orally, intramuscularly, subcutaneously or as implants or intravaginally as an impregnated pessary or sponge. The latter method is most preferred because of the ease of administration and the rapid withdrawal of progesterone on removal of the sponge that favors a higher conception rate.^{25,28} In France about 45,000 does were synchronized in 1981.^{6b} Does may be inseminated with large numbers of spermatozoa 31 and 48 hours after pessary or sponge withdrawal and PMSG injection. Further large scale field trials with various combinations of progestogens, PMSG and prostaglandins are indicated. Vaginal progestogen pessaries and PMSG are neither approved nor available in the U.S. for synchronizing does. Furthermore, fertility at the first estrus after certain types of progesterone administration, oral and intramuscular, is reduced even if larger numbers of spermatozoa are inseminated.²²

Pathological Changes in the Reproductive System of the Doe

Anatomic defects of the genital tract of female goats are rare except for a high incidence of intersexes, or pseudohermaphrodites. This was discussed in Chapter III. Hermaphroditism was noted most commonly in polled goats of Swiss origin.^{2,3,78} In one Saanen herd the incidence of pseudohermaphrodites, was as high as 11 percent; in a Toggenburg herd the incidence reached 6 per-

cent. The intersexes are usually male pseudohermaphrodites. The condition appears to be inherited as a simple recessive character associated with hornlessness. Horned hermaphrodites are extremely rare, if they occur at all. To eliminate hermaphroditism in a flock, the polled goats that were normal should be mated to horned goats. Freemartins, such as occur in twin births in cattle, are rare in goats.²⁶ Since other anatomic defects or arrests in development such as uterus unicornis, uterus didelphys, persistence of the median wall of the Mullerian duct with a fleshy pillar caudal to the cervix, other arrests in development of the Mullerian duct, and persistence of the hymen may occur in goats they are rarely recorded. Undoubtedly they are highly unusual.

Pathological lesions or diseases of the reproductive system in goats are similar in most respects to those in cattle. Vulvitis, vaginitis, cervicitis, metritis, pyometra, perimetritis, and salpingitis may occur in goats usually as sequelae to dystocia, difficult parturition, retained placenta, and delayed involution of the uterus. These acute or chronic infections in the doe are handled in a manner similar to the treatment for these infections in cattle. In retained placenta, which is much less common in does than cattle, the uterus may be treated locally, preferably with a broad-range antibiotic, and the placenta is allowed to drop away. For a valuable doe a better treatment is to give parenteral antibiotics for 3 to 5 days and not to place any drug in the uterus or to attempt to remove the afterbirth. Manual removal of a retained placenta is not indicated due to the small size of the genital tract.

Infections of the genital tract other than postpartum infections apparently are seldom a cause for infertility in ewes and goats. This may be explained in part by the long period between breeding seasons, in which recovery can take place. Brucellosis, usually due to *Br. melitensis*, is characterized by abortion. Infertility in goats associated with brucellosis is not described. A granular vulvovaginitis in does has been described due to *Mycoplasma agalactiae*.¹⁴ After an incubation period of 7 days, the lesions in the vulva which are similar to those in granular venereal disease of cattle, are observed for several months. The granular papules are accompanied by edema and a mucopurulent exudate. The granular lymphoid lesions were also noticed in the anterior vagina and on the cervix.

Anestrus in does during the breeding season is occasionally observed and may be due to:

1. the intersex condition in naturally-polled does.
2. pregnancy or rarely pseudopregnancy with a persistent CL.

3. hydrometra or mucometra, probably with a persistent CL.
4. severe nutritional deficiencies especially in TDN and protein, or a chronic debilitating disease including external and internal parasitisms resulting in cachexia often with anemia.
5. prepuberal anestrus, usually due to restricted feed intake and anestrus in old does due to inability to chew properly, a restricted diet and heavy lactation.
6. anestrus due to pyometra or cystic ovaries is possible but seldom reported.
7. severe heat stress may shorten estrous periods and reduce the observable signs of estrus.
8. mineral deficiencies of copper, cobalt, phosphorus, and selenium may have a minor role in infertility, delayed puberty and reduced signs of estrus.
9. failure to observe estrus particularly in small flocks without a buck is not uncommon.

Hydrometra or mucometra has been described as a cause of anestrus, infertility and abdominal distention in does. The uterus is distended with up to several liters or gallons of a thin clear fluid but no membranes or fetus are present. The doe usually has a history of mating normally and the owners consider her pregnant. This fluid is often expelled spontaneously about 150 days after service.^{24b,25} The laymen often speak of this as a "cloud-burst" condition. A corpus luteum remains in the ovary during this condition and pregnancy examination with ultrasonography, not the Doppler instrument, will often erroneously indicate the doe is pregnant. There is no association in hydrometra with evidence of a fetus, cystic ovaries or an obstructed cervix. The report of a hydrops condition in ewes with permanent sterility caused by phytoestrogens and a persistent CL after mating¹ would lead one to speculate that this condition in does is due to a failure of the production of prostaglandin, the uterine luteolytic substance, and a persistence of the CL. A plasma progesterone assay is probably indicated. If this is the case and a high progesterone plasma level is present, the administration of prostaglandins, 2 to 3 mg. of PGF_{2α} or 100 to 150 ug. of cloprostenol should cause luteolysis and expulsion of the fluid. The prognosis for the future reproductive life of the doe is good. One doe was cited that had alternate normal and false pregnancies for 6 years.^{26b}

Cystic follicles or ovaries have not been described in does. The normal Graafian follicle is about 1 cm. in diameter. Larger "follicles" up to 3.7 cm. in diameter have been reported in abattoir specimens.²⁵ These may be parovarian cysts, cystic ovarian tumors, bursal cysts, or

larger than normal follicles. Short cycles in does especially early or late in the breeding season are common and not an indication of a pathological endocrine problem. Treatment is not indicated.

Intersexes or hermaphrodites are commonly observed in naturally polled does. These intersexes are genetic females and although the polled condition is dominant the hermaphroditic defect is recessive, sex-limited and incompletely penetrant. (See Chapter III.)^{2,3,22,25} Prevention of this condition is assured if either the sire or dam is horned. Most of these hermaphrodites are phenotypic females most with ootestes and many exhibit a projecting vulva and enlarged clitoris. The more masculine phenotypes have a penile-like clitoris, hypospadias and hypoplastic testes often in the inguinal region. Variable development or lack of development of the mesonephric and paramesonephric ducts are seen at autopsy. The vagina in these hermaphrodites is very hypoplastic and a small glass rod will only penetrate about an inch past the vulva.¹¹

A **caprine freemartin** with XX-XY chimerism was described.²⁶ It resembled a male pseudohermaphrodite with an enlarged clitoris and inguinal testis-like gonads. Goat X sheep **hybrids** have been produced. Does (60 chromosomes) bred to rams have greater fertility than ewes (54 chromosomes) bred to bucks. Early development of the embryo is normal but at the time of placentation a possible immunorejection response may occur resulting in early fetal deaths from 40 to 60 days of gestation.²⁵

Reproductive efficiency in Angora goats is very low under range conditions compared to the other caprine breeds and the net kid crop per year in the U.S. is about 50 percent vs. 100 to 200 percent for the other breeds. This low rate is possibly due to poor nutrition but most likely due to selection practices and the stress of high mohair production. In range flocks predators and cold stress also reduce the kid crop.^{22,23,25} This condition in Angora goats has been intensively studied in South Africa.²⁹⁻³¹ It is characterized by the selection of larger kids with finer hair coats that produce more high quality mohair until 3 to 5 years of age. This was also associated with a better breeding potential of both does and bucks the first breeding season. These selected animals usually had small adrenal glands and low plasma cortisol levels. Such selective practices would make these animals with adrenocortical hypoplasia more susceptible to nutritional, physical, climatic and gestational stresses.

After about the fourth or fifth year of life the incidence of abortion increased markedly. Most abortions occur from 90 to 110 days of gestation and were associated with

evidence of growth retardation and anemia of the fetuses and fetal adenocortical hyperplasia with excessive estrogen secretion. This was usually preceded 10 or more days by a severe reduction in maternal plasma cortisol levels along with maternal adrenocortical atrophy. High nutritional levels during this period protected most habitual aborters from losing their fetuses. With our present knowledge an hypothesis might be proposed that this triggers prostaglandin release, involution of the corpus luteum and abortion similar to the sequence of events at parturition. Older habitual "aborters" tended to develop adaptive changes of enlarged pituitary glands, adrenal hyperplasia, high plasma cortisol levels and hyperadrenocorticism, with poor hair growth, and abdominal distention. In Angora goat flocks a minor peak of early abortions was noted at 34 to 46 days of gestation and in these does fetal mummification or maceration occasionally followed fetal death and delayed evacuation of the uterus. Controlling this problem in Angora goats requires careful genetic selection by eliminating aborting does and their progeny. Bucks should be selected from nonaffected strains or families. Abortion, although common, was not identified as the major cause of low reproductive efficiency in Angora goats in Texas. Adequate nutrition including supplemental feeding, parasite and infectious disease control, shelter in inclement weather and predator control are further required management practices.²³

Tumors of the genital organs of goats are rare.^{9,25} Granulosa cell tumor and dysgerminoma of the ovary have been reported. Uterine tumors include adenocarcinoma, leiomyomas and fibromas. Rare adenomas and fibromas of the vagina and vulva have been described. As in cows, squamous cell carcinoma of the vulva and perineum is not uncommon in white-haired does exposed long periods to sunlight. Although lymphosarcomas are reported in goats the genital tract is apparently seldom involved. Warts and melanomas are occasionally seen on the perineum.²⁵

Ectopic mammary tissue in the vulva of does is characterized by a firmness and swelling of the vulvar lips prior to parturition that regresses in several months. Aspiration of milk or a biopsy confirms the diagnosis. Rarely these swellings at parturition may interfere with defecation and urination.²⁵

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Chapter XVII

INFERTILITY AND REPRODUCTIVE DISEASES IN BITCHS AND QUEENS

by Donald H. Lein, DVM, PhD*

In the last ten years, significant studies in reproductive physiology in the bitch and queen have taken place. Learning the normal female reproductive physiology and endocrinology of both these domestic small animal species has helped understand the infertility problems that may be due to misinterpretation and lack of knowledge of the normal reproductive cycle, as well as those irregular cycles that are abnormal physiological patterns. Still more research in the pituitary gonadotrophins, gonadotrophic releasing hormones, endogenous prostaglandins, influence of higher brain centers on reproductive hormones as well as the influence of other endocrine hormones on the reproductive cycle is needed. This decade has certainly noted the influence of hypothyroidism on the cycle and reproductive performance of both the female and male dog and to a certain extent the queen. The genetic effect of certain breeds in both species also plays a significant role in their reproductive performance since selection, small gene pools of certain breeds, close line breeding or inbreeding are all frequently potentiated by breeders.

New hormone products to treat infertility problems, especially prostaglandin F_{2a} (PGF_{2a}), analogues of PGF_{2a} , gonadotrophic releasing hormone, (GnRH), and the bromoergocryptine drugs have just recently began to be used in these two species to treat infertility problems. Use of hormone products to influence the cycle in both species is still largely empirical and controlled by observed or expected clinical effects. Use of hormones, antihormones, immunological measures and other unique methods for cycle and reproductive control and widespread inexpensive sterilization of pet populations still needs in depth research and field trials.

The clinical study of infertility in the bitch and queen have been enhanced by careful methodical examinations over a period of the reproductive cycle time, with good

adequate histories and clinical records. Use of veterinary diagnostic endocrinology laboratories for hormone profiles, vaginal cytology and good veterinary clinical practices including vaginoscopic examinations, sexual behavior records, deep vaginal cultures, laparoscopic examination, hysterosalpinography, ultrasound and good client education has greatly enhanced the success of diagnoses and treatments of infertility in these two species. The veterinary profession and several veterinary colleges and private clinics have made small animal theriogenology a specific service or entity much like that for our large domestic animal theriogenology services.

Infections of the reproductive tract are common in both species and in recent years have been studied and characterized further, leading to the successful treatment of selected cases to restore fertility. Tumors of reproductive organs and mammary glands, hyperplastic and degenerative reproductive tract lesions and their association with both exogenous and endogenous sex steroid levels have been further elucidated. Several recent excellent review articles on small animal reproductive physiology, endocrinology, pathology and infertility have been published and the reader is encouraged to review this list at the end of this Chapter.

Canine Reproductive Physiology

Puberty in the bitch occurs as early as 6 months of age and rarely as late as 22 months of age with most bitches showing their first estrus between 8 to 12 months of age. The plane of nutrition and other stress or disease factors may influence the onset of puberty as in other species. In general, small breeds of dogs exhibit earlier puberty than large breeds. Confined dogs reach puberty later than free-roaming dogs and single confined dogs may reach puberty later than groups confined together. (See pages 409-411.)

Onset of puberty is gradual with interrelated changes in hormone levels and reproductive development. Some bitches apparently have several abortive attempts at estrous expression. Endocrine studies show that individual

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pubertal bitches have inadequate or sporadic elevations in estradiol-17B blood levels during the preovulatory phase of the cycle that are associated with reduced or abbreviated LH surge blood levels and this leads to an absence or only minor preovulatory rise in serum progesterone which is also associated with a lack of sexual receptivity.^{27,139} Bitches may show vulvar swelling, bleeding and attract males because of brief elevated blood estrogen levels from early follicular activity prior to a full estrous cycle. In studies on the Beagle bitch by Anderson and Simpson, a few showed false estrus at 6 and 9 months of age with short periods of proestrus (2 to 5 days) during which time the female attracted but would not accept the male.³ These bitches usually showed estrus in the next few weeks. Puberty in these Beagle bitches occurred at approximately 12 months of age with the youngest being at 8 months. In one study, the mean duration of proestrus and estrus was significantly shorter in bitches experiencing the first reproductive cycle than in those experiencing the second. The ability of bitches to demonstrate normal sexual behavior at the first estrus appears to be a function of age and not size.¹³⁹

Asdell cited Schotterer in reporting that ovaries of female pups at birth contain 700,000 oocytes; at puberty there are 355,000, at 5 years of age nearly 40,000 and at 10 years of age only about 500 follicles remain.⁵ In another report, the ovary of a 2 month old Beagle contains approximately 100,000 follicles and thereafter the number progressively decreases so that at 8 years of age only about 2000 follicles are present.³

The genital ridge is first recognized in Beagle embryos of 7 to 9 mm in crown-rump (C-R) length.³ Histologic evidence of the testis and ovary are recognized in 20 mm and 30 mm embryos, respectively. By late gestation, oogonia and pregranulosa cells are present in the cortex of the ovary with no evidence of prophase meiosis until after birth. Primary follicles become more abundant as prophase meiosis wanes and ceases in Beagle pups between 33 and 54 days of age. Any oogenic foci found after this time appear to be presumptive and abortive centers of oogenesis. Polyovular primary follicles, that is follicles with 2 or more oocytes surrounded by a common granulosa, are first observed at 81 days of age and become a prominent feature of the dog ovary.³ Most primordial germ cells, primary or vesicular follicles undergo atresia with only relatively few reaching maturity, ovulation and formation of corpora lutea. As the bitch ages the ovary develops surface crypts which increase and may be used to distinguish prepuberty, maturity, middle and old age.³

If a bitch is well grown, there is no reason not to breed on the first estrus. Full sexual maturity, the attainment

of maximum capacity, may not be fully attained until the second or third estrus.¹⁰⁹ Beagle bitches in one study reached a reproductive peak at 3 years of age.³ By 8 years of age, reproductive senility was present, with longer interestrous periods, increased infertility and increased preweaning mortality.

The estrous cycle—The dog is considered a monestrous animal with only one estrous cycle occurring during the breeding season. In a review by Shille and Stabenfeldt, an even distribution of estrous cycles throughout the year was shown, although there is definite pattern of increased incidence of estrus from January through May.¹⁰³ There are some reported breed differences, with the Basenji bitch having the highest birth rate from November through January although pregnancies and estrous cycles occur throughout the year in this breed.¹⁰³ Greyhounds and other large breeds may have only one estrous period a year.¹⁸ (See pages 411–415.)

The interestrous interval is affected by breed differences, but not necessarily by breed size. There appears to be less variability within animals than within the breed. Studies on several breeds showed interestrous interval differences for the Toy Poodle of 239 days, Cocker Spaniel, 186 days, Basset Hound, 175 days, German Shepherd, 149 days, and Rough Coat Collie, 255 days.^{103,115} Differences for the same breed but in different localities have also been reported: Great Britain versus the United States, Cocker Spaniels, 224 vs. 186 days, Miniature Poodle 189 vs. 239 days, respectively.¹⁰³

In some studies, the interestrous period appears to be lengthened following pregnancy versus a nonpregnant cycle, while other studies have shown no significant differences.^{27,103,115} Further studies on the interestrous period are needed on the effect of pregnancy versus nonpregnant cycles and the effect of breed, husbandry, nutrition and environment. Latitude and photoperiodicity had no effect on the reproductive activity in dogs in Great Britain.²³ Age does affect the interestral period with increased interval time and more irregular cycles.

Bums and Fraser quoted Frost in reporting that in nearly 500 bitches, 338 had an estrous interval of 5 to 7 months, over 100 had an interval of over 7 months and only 16 had an interval of less than 5 months.¹⁸ In other studies, the interval averaged between 7 to 8 months and 4 to 13 months (over 7 mo.) in a Beagle colony.^{27,103} Intervals longer than 13 months always had an intervening ovulatory and luteal phase for which no sexual behavior was observed, a silent heat, but was detected by serial progesterone blood levels.^{27,34} In the author's experience, interestral periods less than 4 months are usually irregular or abnormal cycles with no ovulations, luteinized cystic follicles or very short luteal function. The interval

between estrous cycles is rarely 6 months, so most bitches have the ability to be in estrus or whelp in any month of the year.

The estrous cycle of the dog as originally described using the four terms, anestrus, proestrus, estrus and metestrus are still used and accepted.^{3,27,34,62} Metestrus was used to designate the full luteal phase. The terminology used in other domestic animals; metestrus, the period of luteal formation to maximal size or maximal progesterone production, and diestrus, the period of maintenance of the mature corpora lutea, is difficult to use in the bitch, since these stages may be looked at differently by sex behavior, estrogen and progesterone blood levels, and vaginal cytology. Concannon, et al., has shown that progesterone is produced by the mature graafian follicle prior to ovulation and is responsible for initiating sexual receptivity in the bitch.³³ Also, the bitch is sexually responsive to the male well after ovulation and into early formation of the corpora lutea with high progesterone levels. Thus, metestrus and estrus in the strictest sense overlap or occur within each other. Maximal blood progesterone levels do not occur until 15 to 25 days after the LH peak and the nonpregnant bitch may continue to secrete progesterone above basal anestrus blood progesterone levels for 120 to 150 days after the LH peak.

Holst and Phemister observed a sharp decline in vaginal cornified cells about 3 days before the end of behavioral estrus and suggested that this be considered the first day of diestrus.^{55,56} They also found in a later study that vaginal cornification was complete in 12.1 days (S.E., 0.2) from the beginning of estrus and 8 days (S.E., 0.3) from the LH peak. They considered this stage of the cycle should be diestrus. Behavioral-wise the bitch may still be in estrus, the corpora lutea are still developing, progesterone levels are still rising for some days and in the strict scientific sense this stage is metestrus.

Stabenfeldt and Shille suggested that the simplest approach is to recognize that metestrus occurs during the latter part of estrus in the dog and to use the term diestrus for the luteal phase of cycle which begins with the loss of sexual receptivity.⁴⁷ A nomenclature committee of small animal theriogenologists, endocrinologists and physiologists must finally decide on an acceptable terminology for all to use.

The estrous cycle of the dog is considerably longer and more variable compared to our large domestic animals. In general, the four accepted phases or time periods are: 9 days for proestrus (range 3–16), 9–10 days for estrus (range 4–12), 75 days for metestrus-diestrus (range 51–82), and 125 days for anestrus (range 15–265).¹¹⁷ The less variable portion of the estrous cycle is proestrus-estrus which is frequently quoted as 21 days

of attraction followed by loss of receptivity to the male. The most variable are metestrus-diestrus and anestrus.

Vaginal cytology, If used on a routine basis in a cycling bitch can accurately reveal the stages of the estrous cycle. Vaginal smears examined at one- to two-day intervals during proestrus, estrus and early metestrus/diestrus can be a very valuable clinical test to predict when a bitch will ovulate, when to inseminate or send to a stud for breeding, or when an irregular cycle is taking place. Couple the vaginal cytology with sexual behavior, teasing with a sexually active male, changes in the size and consistency of the vulva, changes in the vaginal and cervical mucosal folds and possible sex steroid hormone serum profiles and the strength of clinical diagnostic and management at breeding for optimum reproduction greatly increases. (Chart III) The above tests and changes are all under the influence of estrogen and its mitogenic

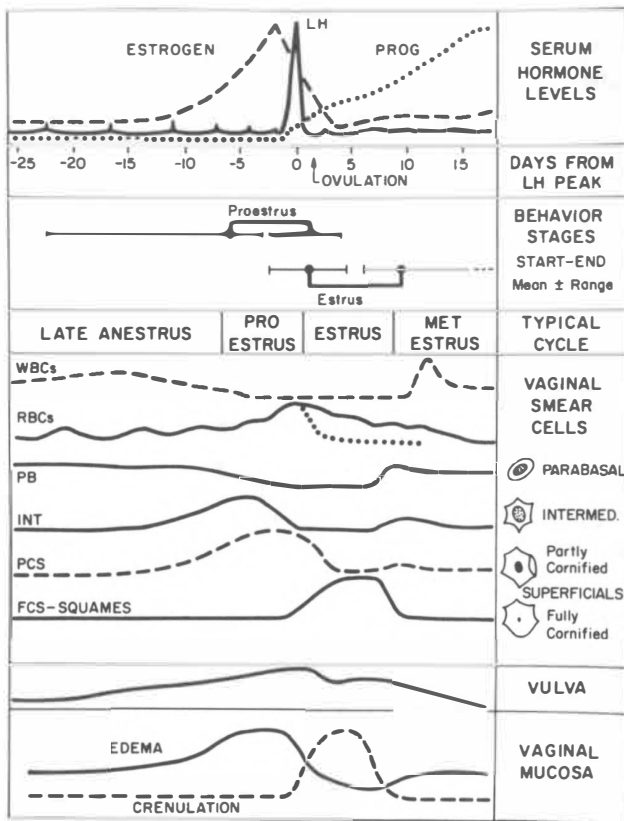


Chart III. A schematic summary of temporal relationships between periovulatory endocrine level changes, behavioral, vaginal exfoliated cytology, vulval and vaginal mucosal changes associated with the estrous cycle in the bitch. (Courtesy and with permission of P. W. Concannon and publisher, W. D. Saunders, Co.²⁷)

influence especially on target tissues. Several excellent reports have been published on the obtaining of specimens, stains and techniques for staining, interpretation and correlation of vaginal cytology to the estrous cycle, reproductive hormone changes, sexual behavior, reproductive tract changes and diagnostic use for infertility conditions in the bitch.^{2,8,22,27,42,55,64,68,87,88,98,100,102,117,122}

Specimens must be collected from the vagina and not the vestibule since cells from this area do not readily reflect sex steroid hormone changes and are always cornified.^{42,98} Thus, the use of a speculum is important to bypass the vestibule. No lubrication for the speculum or collecting instrument should be used since most cause artifacts on the smear. Specimen collection can be done with a moist clean cotton swab, metal or wood spatula, glass rod, pipette and saline flush; the author prefers a moist (saline) clean cotton swab which is rotated in the anterior vagina. Cells are less distorted if the swab is rolled on the clean glass slide instead of pulling across the slide. Several stains are available; Wright's, Leishman's, Giemsa, Wright's-Giemsa, Trichrome stains such as Sano-Pollack Trichrome,⁹⁸ Shorr's trichrome, New Methylene Blue, Toluidine Blue and Diff Quick, a modified Wright's-Giemsa stain.^{27,87} The author prefers to use Diff Quick because it is simple, rapid and adequate and the slides can be stored for reference and studied throughout a bitch's cycle. A drop of New Methylene Blue on a cover slip, applied to an air-dried vaginal smear can be read immediately and shows good detail, but it will not stain red blood cells and cannot be stored for reference.^{68,87} It is advisable to stay with one stain throughout a study of an estrous cycle because of the difference in staining detail between stains.²⁷

An excellent study on the changes of cells and cell types with percent of changes throughout the cycles is reported by Christie, et al.²² Increasing estrogens from the developing follicles during proestrus and estrus cause the target tissue of the vagina to progress rapidly from a two cell thick epithelium in anestrus, made up of basal and parabasal cells that are small round cells containing a large distinct nucleus, to a very rapid growing epithelium that will become several cell layers thick as estrogen levels increase in late proestrus. Cells as they mature from basal and parabasal cells will become larger, lose their round shape and become polyhedral or angular, still contain a nucleus (called intermediate cells) and eventually become larger, more polyhedral and degenerate so that the nucleus now becomes pyknotic, eventually lysing (karyolysis) and disappears. These cells are classified as superficial cells, containing a pyknotic nucleus, partly cornified, or anuclear, fully cornified. The completely cornified superficial cells are seen with the full effect of high estrogen levels and are predominant in the

smear when the height (number of cell layers) of epithelium is maximum. These cells are polyhedral, frequently "wrinkled" or "curled" and appear like "corn-flakes."^{130a} The cytological change, day by day, through the early cycle (proestrus, estrus, early metestrus) is always a percentage of change in types of cells. Late in anestrus, mainly scant parabasal and early intermediate cells are present. Occasionally in the last 40 or 50 days of anestrus, erythrocytes will be seen in the smears before any vulvar bleeding at proestrus is noted indicating early follicular activity and estrogen production.¹²² Proestrus is characterized by mixtures of parabasal, intermediate and superficial cells (cornified cells) that progress towards a higher percentage of mature or completely cornified cells in late proestrus to early estrus. Erythrocytes, from uterine diapedesis are quite numerous in proestrus, tend to decrease in estrus, but in some bitches, may be present through estrus and into metestrus/diestrus. The presence or absence of erythrocytes in estrus or diestrus is the most variable of all cell types. Leucocytes, polymorphonuclear leucocytes, are present in proestrus, but are not present in full estrus. If they are present, it indicates an inflammatory process in the reproductive tract and they are usually degenerate leucocytes filled with phagocytized bacteria. Epithelial cell changes and height (number of cells thick) of epithelial layers in the vagina during proestrus and estrus follow estrogen secretion levels by approximately 1–2 days, thus maximum cornification (95–100%) follows the preovulatory LH surge by 1–2 days.^{27,102,103} Near the time of the LH peak, a clearing of the background on the glass slide (lack of debris) takes place and is possibly related to a decrease in mucoprotein content of the vaginal mucus.^{27,68} This is usually an optimal time to start breeding a bitch or to send the bitch to a breeder, since LH release has taken place and destined ovulation is eminent. Shipping and changing of the environment of bitches prior to destined ovulation may cause a bitch not to ovulate because of inadequate LH-RH, LH release, possibly controlled and blocked by the higher brain centers. The "clearing" effect is best noticed when following a series of daily or every other day vaginal smears. By 3 or 4 days after the LH peak, fully cornified superficial cells (anuclear) almost completely replace partially cornified superficial cells (contain pyknotic nuclei). About 7 to 8 days after the LH peak, an abrupt decrease in cornified epithelial cells takes place, confirming retrospectively that ovulation has taken place. There is a rapid loss of fully cornified epithelial cells and reappearance of intermediate and parabasal cells indicating the start of metestrus or the onset of diestrus as described by Phemister, et al.⁹¹ This is probably the last day that an unmated bitch is likely to be fertile since it coincides with the

fertile lifespan of oviductal oocytes.²⁷ The reappearance of leucocytes in the vaginal smear in early metestrus/diestrus indicates the end of the fertile period and the increase of progesterone blood levels. The reappearance of leucocytes may coincide with the metestrus/diestrus shift of epithelial cells, but frequently their entrance are more variable and may be one or two days earlier or in the author's experience, two to four days later and in many cases may not be that abrupt in appearance. If a bitch is presented at this time with no prior history of stage of cycle, by either behavior or vaginal cytology, this stage (early metestrus) may be confused with proestrus. Study of further daily smears will determine the stage of the cycle. As the bitch proceeds into late metestrus/diestrus, the cell thickness (number of layers of cells in vagina) returns to 5 to 8 cells thick and eventually to two or three cells thick at anestrus. In a study during metestrus and anestrus, Dore described the great increase in parabasal and intermediate cells after 30 days postovulation which increased in late metestrus/diestrus and early anestrus to mainly parabasal cells. Recognition of this stage is important when a bitch of unknown cycle status is presented for contraceptives or for estrus induction (Chart III).

Vaginal smears for cytologic diagnosis of inflammatory processes of the genital tract; vaginitis, endometritis, pyometritis, or subinvolution of placental sites versus postpartum metritis or endometritis, neoplasia, etc. are well described by Rozzel and a recent report by Olsen, et al.^{88,98}

Vaginocopy or endoscopy of the vagina of the bitch has been a very valuable procedure for pinpointing the changes from proestrus to estrus and finally metestrus/diestrus. This procedure is also useful for breeding soundness examinations and the diagnosis of anatomical abnormalities, inflammation, neoplasia, obstetrical and postpartum difficulties.^{27,68,69,70} Lindsay has described the method used for postuterine endoscopy and the estrous cycle changes. Visualization of the vaginal mucosa can best be accomplished with a fiberoptic proctoscope or sigmoidoscope (Welch-Allen) in both noninflated and insufflated states. These instruments can easily be passed with sterile lubricant to the anterior vagina and a complete examination performed with minimal restraint of the bitch. The true cervix cannot be easily viewed because of the anterior dorsal median vaginal fold which occupies the anterior 2 or 3 cm. of the vagina and narrows this portion of the vaginal cavity to a ventral slit, making it difficult to pass instrumentation in this area unless it is 4 mm in diameter. The true cervix opens on the anterior ventral portion of this dorsal fold. A paracervix, which is the caudal portion of this dorsal vaginal fold and contains

the narrowed ventral lumen leading to the true cervix, is frequently mistaken for the external cervical os.^{27,68,69,70,93}

The cervix can be seen easily in full estrus or at late pregnancy, at whelping or early postpartum when the area is under the influence of estrogen, is edematous and quite dilated. As estrogen increases during proestrus, the vaginal mucosal folds become progressively more edematous, rounded, puffy and turgid in appearance. At the time of the preovulatory LH peak, estrogens are falling, progesterone is rising, the blanched, rounded, smooth mucosal folds and prominences that completely fill the vaginal lumen quickly change and rapidly develop a wrinkled, angular, peaked or crenulated appearance that are less edematous and do not fill the vaginal lumen. It is felt that these gross changes probably reflect an abrupt withdrawal of the water retention effects of estrogen during the preovulatory decline in estrogens and the triggering of the LH peak. This is the start of estrus and coincides with acceptance of the male and complete cornification of vaginal cytology. The angular or crenated vaginal mucosal folds will continue to be present for 5 to 6 days and then are lost about the time of the metestrus/diestrus shift in the vaginal cytology and are replaced by flaccid vaginal folds with the paracervix area appearing as a soft "rosette." These changes can easily be followed through proestrus, estrus and early metestrus/diestrus by every other day examinations (Chart III).

Progressive swelling and edema with turgidity of the vulva, perineum and the ventral floor of the caudal vagina takes place with increasing estrogen levels in proestrus. Frequently this edema is ascertained prior to vulvar bleeding in early proestrus. Since these are target tissues for estrogen and easily visualized and palpated, daily examination of the vulva will give a good indication of the progression of proestrus and the change to estrus because the rapid decline in estrogen levels will cause a rapid softening of the vulva and vaginal floor at estrus. This is an ideal time to breed the bitch. Some bitches could not be naturally bred in late proestrus because the vulva and hypertrophied caudal vaginal floor are so edematous and enlarged. In some bitches, severe edema and hypertrophy of the vaginal floor will lead to prolapse of the hypertrophied caudal vaginal floor between the vulvar lips.

Endocrinology of the estrous cycle and pregnancy—Excellent studies and reviews on the endocrinology and physiology of the estrous cycle and pregnancy of the bitch have been reported.^{3,20,24,26,27,30,31,33,34,35,36,37,38,40,47,}

^{53,54,62,70,74,75,77,79,82,84,85,91,94,95,102,103,106,108,109,116,117,119,}

^{120,121,123,124,125,127,128,136,137,139} The follicular phase, mainly proestrus and early estrus was considered an abrupt occurrence following a quiescent anestrus. Olson, et al. has shown that in late anestrus (at least 45 days before proes-

trus) concentrations of follicle stimulating hormone (FSH) in serum are high (240 to 294 ng/ml) and again at the time of the preovulatory surge of luteinizing hormone LH (297 ng/ml). During proestrus, FSH was lowest (131 to 200 ng/ml). There is sufficient FSH present during anestrus for follicular growth.⁸² Serum estradiol 17-B was high in late anestrus (20 to 46 pg/ml), decreased prior to proestrus (8 to 46 pg/ml), and increased through proestrus and then dropped just prior to estrus. Inhibition of FSH may be caused by elevated estrogen levels (negative feedback) or, as proposed for other species, elevated serum levels of inhibin a follicular peptide that selectively inhibits FSH secretion.²⁷ The serum LH levels were inverse to the estrogen levels, low early, higher just prior to proestrus, possibly inducing a new follicular phase, lower during proestrus, and then surging to a high level at estrus. Similar findings for LH and estrogen were found in prepuberal bitches prior to their first estrus.¹³⁹ Concannon has also noted that in nonpregnant bitches in anestrus (150–180 days from last estrus) ovarian follicular activity, uterine and oviductal hyperemia, including enlarged fimbria and a congested red endometrium are present. He believes this represents the transition from late luteal phase of one cycle to the early follicular phase of the next cycle.²⁷ Others have also reported this phenomena in pubertal and anestrus bitches.^{3,116} From the above reports, anestrus cannot be considered strictly a quiescent state.

At the onset of proestrus, several follicles, 1.0 to 1.5 mm in diameter are present on the ovaries of Beagle bitches. They increase to 2 mm by mid proestrus, 3 to 4 mm by late proestrus and 3 to 5 mm by the onset of estrus.³ Several of these follicles degenerate at any of these stages, while a few, up to 20 or more, increase to 8 to 10 mm in diameter at ovulation.¹³⁷ Mature follicles are amber in color, contain several infolds of the granulosa cell lined wall and coiled blood vessels can be seen in the walls. Just prior to ovulation, the oocyte becomes free-floating in the follicular fluid. The rupture site of a follicle can be recognized by a pinpoint area with very scant hemorrhage and no appreciable collapse of the walls.³ The released oocytes promptly pass to the ampullary region of the oviducts. The turgid fimbria effectively close the ovarian bursa (ventral slit) at ovulation to prevent the loss of ova.

During the follicular phase, estrogens cause the increasing evidence of external signs of proestrus: edema, hyperemia and enlargement of the vulva, vaginal discharge of uterine blood (endometrial diapedesis), edema and hypertrophy of the caudal vaginal floor, secretion of sex pheromones from the vaginal or vestibule secretions and attraction of males. Urine from bitches in proestrus

and estrus will attract males at this time.⁴³ One vaginal sexual attractant was analyzed as methyl-p-hydroxybenzoate.⁵¹ Methyl-p-hydroxybenzoate and to a lesser extent, propyl-p-hydroxybenzoate, when applied by cotton swab applicators to the vulva and vestibule of anestrus or ovariectomized bitches caused intense anogenital interest and attempts at mounting by teaser males. The use of oral administration of chlorophyll in some bitches at the first sign of proestrus appears to mask the sexual attractive odors of bitches in proestrus/estrus.¹⁰³

During proestrus, the bitch will usually not permit mounting and intromission. The behavioral change from proestrus to estrus is when the bitch will stand for the male, with tail deviated laterally and the back in a lordosis position. This is also the time when vaginal cytology has changed to mostly cornified epithelial cells with no leukocytes and lack of debris and variable amounts of red blood cells. At this time the vulva has come from a full swollen, turgid, edematous estrogen-primed tissue to a more flaccid, soft tissue with a rapid decrease in estrogen blood levels and increasing progesterone blood levels. The tumescence of the vulva of most bitches during proestrus would make intromission by the male almost impossible even if the bitch would stand. Daily vaginoscopic examination at this time also shows a change in the anterior vaginal longitudinal and transverse folds and the paracervical areas from a smooth edematous rounded swollen, "pillow" type appearance to an angular, sharp edged or crenulated, wrinkled appearance. These changes take place when serum estrogen levels are falling and early progesterone levels are increasing and indicate the luteinizing hormone (LH) surge that will cause ovulation in the next 2 days.^{69,70} This abrupt change is one of the best clinical signs to indicate the LH surge and ovulation (Chart III).

The endocrine and reproductive patterns during proestrus and early estrus have been well defined by several investigators.^{3,20,24,27,31,33,34,38,47,53,62,74,75,77,82,84,91,94,95,102,103,106,107,109,136,139} The serum estradiol 17-B levels increased from basal levels of 2 to 10 pg/ml to peak levels of 50 to 120 pg/ml in late proestrus.²⁷ Concurrent increases in estrone also take place with these levels being elevated during the 6 day interval both before and after the LH peak, while average estradiol-17-B levels remain elevated only during the 6 day interval preceding the LH peak.¹³⁹ The release of LH to cause ovulation is initiated by the drop of blood estradiol-17B and that is facilitated by the low, but rising blood progesterone levels.^{27,31,33,34,38} Sexual receptivity in the bitch is the result of a slight preovulatory rise of serum progesterone in association with a preovulatory serum LH surge and a rapidly declining serum estradiol-17B level.^{27,38} The source

of the progesterone appears to be the preovulatory luteinizing granulosa cells of the mature follicles (Chart IV).

Further work with ovariectomized Beagle bitches showed that the best combination of sex steroid hormones for inducing estrus was to administer estradiol-17B for 8 days followed by progesterone and removal of estradiol-17B.^{31,33,38} The mechanism of regulating LH release in the dog appears similar to that of other species, mainly gonadotrophin releasing hormone (GnRH) from the hypothalamus which releases both LH and FSH. Exogenous GnRH causes LH release in the bitch within minutes.¹⁹

Atypical reproductive behavior and patterns are observed in certain bitches at estrus. These atypical responses include lack of sexual receptivity and reduced or inconsistent patterns of circulating concentrations of estradiol-17B, luteinizing hormone (LH) or progesterone. It appears that inadequate or sporadic elevation in levels of estradiol-17B during the preovulatory phase of

the cycle were associated with reduced or abbreviated LH surge concentration which resulted in a minor preovulatory rise in serum progesterone causing a lack of sexual receptivity.¹³⁹

Olson, et al. has reported that during proestrus, mean serum testosterone levels range from 106 ± 29 to 239 ± 3 pg/ml with a high concentration of 526 ± 225 pg/ml occurring the day of the preovulatory surge of LH. During late anestrus, levels of serum testosterone ranged from 31 ± 11 to 141 ± 63 pg/ml. The physiological or endocrinologic function of testosterone in the bitch has not been studied.⁸⁴

Ovulation is spontaneous in the bitch and occurs about 24–48 hours after the LH peak with a range of 24 to 72 hours.^{27,34,91,136} In relation to estrus or acceptance of the male, ovulation has been reported by laparoscopic examination to occur from the first to the seventh day of estrus with one bitch ovulating on the ninth day.^{119,136} Studies on the preovulatory LH peak and the onset of estrus indicate that the latter occurs between 7 to 8 hours

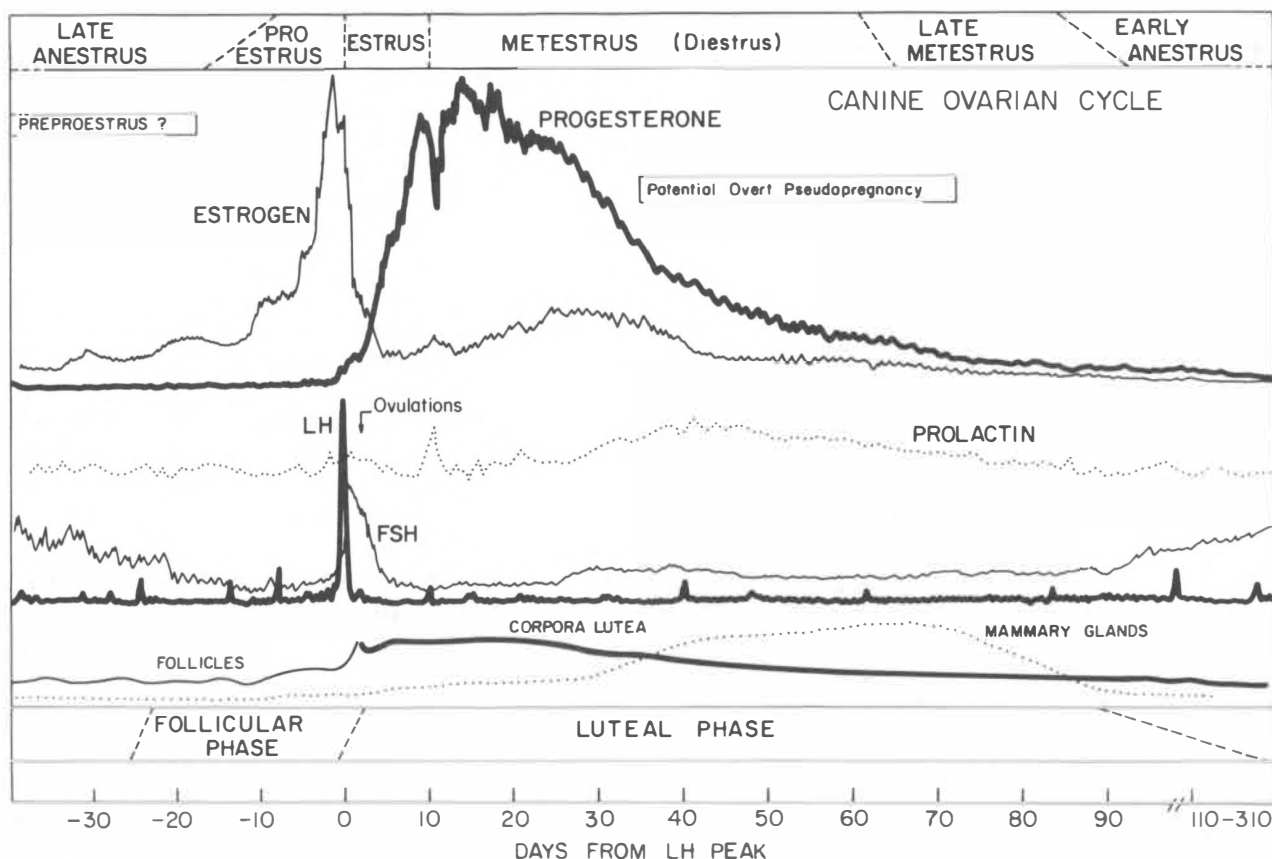


Chart IV. A schematic representation of typical endocrine changes reported, or presumed to occur, during the nonpregnant canine ovarian cycle and their relation to observable stages and functional phases of the cycle.

(Courtesy and with permission of P. W. Concannon and publisher W. D. Saunders, Co.²⁷)

after the LH peak with a range of 3 to 5 days before the LH peak to as late as 4 to 5 days after the LH peak.²⁷ One bitch was reported to have been in estrus 9 days before the LH peak.¹³⁶ "Early estrus" may be caused by a slight or transient drop in estrogen levels or a rise in progesterone during the follicular phase prior to the final estrogen peak. The later estrus, following the LH peak, may occur in an insensitive bitch and is seen particularly in the pubertal bitch. Occasional bitches never show estrus, or even proestrus, and still ovulate. Some of these conditions may be the degree of knowledge, talent and time spent by the observer on canine sex behavior or the number of mating attempts, compatibility of the dog and preference or experience of the pairs. Estrus in the bitch is typically 6 to 12 days, but it may be short, 2 to 3 days in those showing late after the LH peak, or it may be protracted up to 3 weeks or longer in a few females.

The luteal phase of the canine estrous cycle begins before ovulation with preovulatory luteinization of the granulosa cells and theca interna. Complete transformation of granulosa cells into lutein cells is not observed until 4 to 5 hours after ovulation.³ The serum progesterone level continues to rise during estrus and reaches peak levels of 15 to 80 ng/ml or higher between 15 and 25 days after the LH peak.²⁷ Progesterone levels will gradually decline after reaching a peak and are quite variable in concentration between bitches and in duration in the nonpregnant bitch. This may vary in the nonpregnant bitch from 55 to 110 days before reaching serum levels of 1 ng/ml, but may not reach basal levels of 0.3 to 0.4 ng/ml, until 120 to 150 days after the LH peak (Chart IV). Depending on the definition of metestrus and/or diestrus, the duration can be considered to last about 2 months, as in pregnancy; 2 to 3 months until mammary development associated with physiological pseudopregnancy subsides or near the mean of 80 days, when mean serum progesterone levels are 1 ng/ml or lower, or when serum progesterone levels reach anestrus basal values of 0.3 to 0.4 ng/ml, or at 120 to 140 days, when the effect of progesterone on histologically examined endometrium is no longer evident. In the pregnant bitch, desquamation of the endometrial lining is more extensive and repair occurs about 2 weeks later, 140–155 days post coitus.³ One other steroid, estriol, has been found during metestrus and may play a role in the cycle. Estriol is a weak estrogen and may act as a competitive metabolite, displacing estradiol-17B endometrial receptors.

Throughout the non-pregnant cycle, LH and FSH levels appear to remain at basal levels. FSH rises again late in anestrus, as described earlier in this Chapter, and stimulates late anestrus follicular development. LH and prolactin (PRL) are both pituitary luteotrophic hormones

for corpora lutea maintenance in the dog. Studies show that removal of the pregnant or nonpregnant uterus did not alter maintenance of luteal function in the bitch. Also that serum LH concentration appears to increase as progesterone levels decline indicating that cessation of luteal function does not appear to result from a lack of LH.⁸⁵

Prolactin also is inversely proportional to progesterone secretion. Thus serum prolactin levels rise as progesterone levels decline, which may result in overt behavioral signs of pseudopregnancy in some bitches.^{27,64}

Pseudopregnancy—All nonpregnant bitches will undergo a pseudopregnancy in late metestrus/diestrus which may be covert or overt. The covert type will show no behavioral signs of pregnancy, but will still have endometrial and mammary gland hyperplasia. The overt bitch will have varying degrees of pregnancy signs from milk secretion, enlarged uterus and abdomen, nest making, restlessness and false labor, anorexia, vomiting and the caring for toys, inanimate objects or other animals' young. In some bitches and possibly some breeds, either higher levels of prolactin are released or the dogs are more sensitive to expression of pseudopregnancy.²⁷ Some dogs are triggered into overt pseudopregnancy when blood levels of exogenous progesterone or progestins, or possibly similar blood steroids drop.

A homologous radioimmunoassay for canine prolactin has been developed. Throughout the estrous cycle, basal plasma prolactin (PRL) levels of 2–4 ng/ml remain fairly constant until the end of metestrus/diestrus in non-pregnant bitches, when a rise to 9 ng/ml was noted.⁴⁰ Prolactin is highly lactogenic in the bitch and exogenous administration can maintain lactation indefinitely (Chart IV).⁶²

Prolactin and thyroid-stimulating hormone (TSH) are both released following an injection of thyrotropin-releasing hormone (TRH). Prolactin secretion is controlled by hypothalamic prolactin releasing inhibitory factor (PIF) which may be dopamine. Dopamine agonists, such as bromoergocryptine, can reduce prolactin secretion in dogs as in other species and can reduce the severity of overt pseudopregnancy.²⁷ Bromoergocryptine is not used clinically because of its unfavorable side effects, but new analogues show great promise in treating overt pseudopregnancy.

Growth hormone (GH) is primarily a metabolic hormone, but is also lactogenic in some species. Hypothalamic somatostatin, an inhibitor of GH secretion, and GH releasing factor from the hypothalamus, regulate the secretion of GH. Growth hormone secretion can be elevated by progesterone secretion endogenously, and also exogenously, leading to acromegaly-like changes in

bitches, and alterations in glucose and insulin levels.^{27,29}

The most fertile period in the bitch appears to be associated with the time of the LH peak to 4 days after ovulation.^{27,91,103} Bitches have conceived with single breedings as early as 3 days before and up to 7 to 8 days after the LH peak thus leading to gestation periods of 57 to 72 days.^{27,128} It is usually recommended to breed early followed by services every 2 to 4 days.^{27,87} The best method is to utilize daily teasing with a sexually responsive male and breed when the bitch shows the first good stance, with lordosis and lateral deviation of the tail (so called "flagging"). To increase the knowledge of timing or in lieu of a teasing stud, the use of vulvar changes from tumescence of proestrus to relaxation and detumescence of estrus, daily vaginal cytology and vaginoscopic examination can be used to pinpoint the changes from proestrus to estrus, ovulation and on to metestrus.

Ovulation, fertilization and implantation—Canine ova are ovulated from follicles as primary oocytes about 36 to 48 hours (24–72) after the LH peak. Maturation of oocytes take place in the oviduct and may take as long as 2 to 3 days, so fertilization probably occurs no earlier than 3 days after the LH peak.²⁷ For this reason the immature ova shed by the dog, and fox, remain viable for several days after ovulation before the male and female pronuclei join and cell division begins. Thus in canine ova, sperm penetration occurs while the egg is still a primary oocyte but the sperm head remains quiescent in the vitellus until the second polar body is extruded. In one study, using laparoscopy for determining ovulation, the first polar body was extruded at 48–72 hours post-ovulation, the germinal vesicle (follicular cells) were retained until 24 to 48 hours and no follicular cells were seen at 68 hours. Cleavage began from 72 hours on, in the middle or distal part of the oviduct and ova were in the 2 cell stage at 96 hours, 3–6 cell stage at 120 hours, 8 cell at 144 hours, 8–16 cell stage at 168 hours and 16 cell at 192 hours in the distal oviduct. At 204 to 216 hours postovulation the ova in the morula stage were transferred into the uterus.¹²⁰ (See pages 419–422.)

After ova maturation, the fertile life span is not known, but may be two to three days; since in some bitches, fertilization and pregnancy occurred as late as seven days after the LH peak. Mahi and Yanagimachi found that canine oocytes mature to the stage of germinal vesicle breakdown within 48 to 72 hours of in vitro incubation following removal from follicles. Thus, this process may take as long in vivo. They also reported that dog sperm can penetrate canine oocytes after 7 hours of incubation in vitro and that they can penetrate immature or degenerate oocytes as well as mature oocytes.⁷¹ Dog sper-

matozoa can remain viable in the lumen of the uterus for 5 to 6 days and even to 11 days after copulation.^{27,41} Disappearance of spermatozoa coincided with the onset of metestrus.

Free floating blastocysts have been observed in the uterus between 8 and 20 days postcoitum. Implantation occurs 21–22 days after first acceptance, but may have a range of 17 to 18 days (late estrus mating) to 26 days after mating (early mating, 3 days prior to LH peak).^{27,62}

In a series of 21 bitches studied by TsuTsui, the blastocyst on the 16th day after ovulation (determined by laparoscope) has shed the zona pellucida and was free floating in the uterine lumen. Implantation took place 20.5 to 23.0 days postovulation in bitches allowed to mate from 54 hours preovulation to 108 hours postovulation, respectively. Thus the time interval between mating and implantation was 18.5 to 24.0 days and if dated from the time of fertilization, 18.5 to 19 days post fertilization.¹²³ Future implantation sites are noted as edematous areas of the endometrium (Chart V).³

The number of follicles that mature and rupture may vary from 4 or fewer, especially in small breeds, to 20 or more in the larger breeds. As the bitch ages, the number of follicles maturing and ovulating, as well as litter size will decrease. In a study of 135 mongrel bitches the rate of ovulation was 6.0 ± 1.7 ova (2–12), 2.9 ± 1.4 (0–8) in the right ovary, and 3.1 ± 1.4 (0–6) in the left ovary. There was no statistical seasonal affect. The fertilization rate of all bitches was 88.8%. Transuterine migration showed a tendency for distribution to be equal between both uterine horns.¹²¹

Diagnosis of pregnancy via abdominal palpation is usually possible by day 25 of pregnancy following the last mating, but may be possible by 17 or 18 days when mating occurs late in estrus or not until 26 days after a mating occurring 3 days before the LH peak. The uterine horns are like a "corkscrew" from endometrial hyperplasia and hypertrophy during early metestrus and may be difficult to differentiate from implantation sites or swellings of pregnancy.¹¹⁶ The uterine swellings are about 1.0 cm in diameter at 19 to 20 days after the LH peak, 1.5 cm at 23 to 24 days and 2.0 cm at 27 to 28 days and 3.0 cm at 31 to 32 days. The uterine swellings become more confluent and oblong by day 30 to 35 and are difficult to palpate as individual entities from this time on.²⁷ The amnionic vesicle and developing embryo can be viewed by ultrasound by 20 to 22 days postmating with evidence of fetal heart movement by day 22. In the author's experience, biweekly studies with ultrasound can be used to detect, confirm and record by photography early embryonic and fetal death and resorption. Rendano, et al. demonstrated that fetal skeletons do not

Chart V. Events of Canine Pregnancy Timed in Relation to the Preovulatory LH Peak and to Potential Times of Fertile Matings

Event	Days After the Preovulatory LH Peak*	Potential Range of Days After a Fertile Mating†
Onset of proestrus	-20 to -3	-25 to -2
Full vaginal cornification	-4 to +2	
Onset of estrus	-3 to +5	
Estradiol peak	-3 to -1	
Decreased vaginal edema	-1 to 0	
LH surge and sharp rise in progesterone	-1 to 0	
LH peak	0	-7 to +3
First mating	-5 to +10	
First fertile mating	-3 to +7	
Crenation of vaginal mucosa	0 to 1	
Ovulation of primary oocyte	2	-5 to +5
Oviductal oocytes		
Resumption of meiosis	3(?)	
Extrusion of first polar body	4(?)	
Sperm penetration	3 to 7	0 to 7
Fertilization/pronucleus formation	5 to 7	1 to 8
Degeneration of unfertilized ova	6 to 8(?)	
Two-cell embryo	6 to 8	
Loss of vaginal crenulation	6 to 8	0 to 9
End of complete vaginal cornification	6 to 9	
Return of leukocytes to vaginal smear	7 to 12	
Morulae (8 to 16 cells) in oviduct	8 to 10	
Blastocyst (32 to 64 cells) entry into uterus	9 to 11	3 to 14
Intracornual migration (1-mm blastocysts)	10 to 13	
Transcornual migration (2-mm blastocysts)	12 to 15	
Attachment sites established, zona pellucidae shed	16 to 17	
Swelling of implantation sites, primitive streak formation	18 to 19	
Palpable uterine swellings of 1-cm diameter	20 to 25	17 to 27
Onset of pregnancy anemia	30	
Reduced palpability of 3-cm swellings	32	26 to 38
Hematocrit below 40 % PCV	40	
Hematocrit below 35 % PCV	50	
Fetal skeleton becomes radiopaque	43 to 46	
Radiographic diagnosis of pregnancy	45 to 48	39 to 50
Prepartum luteolysis and hypothermia	63 to 65	
Parturition	64 to 66	58 to 70

*Conservative estimates based on literature reports and unpublished observations.

†Based on fertile single matings from three days before to seven days after the LH peak.

(Courtesy of P. W. Concannon)

become sufficiently mineralized and radiopaque for a pregnancy diagnosis until approximately 46 days after the LH peak or 19 to 20 days prior to parturition.⁹⁷ Uterine enlargement is detectable 35 days prior to parturition. Mineralization of fetuses progresses rapidly with the proximal extremities; forelegs/hindlegs/pelvis, caudal vertebrae/paws, and finally teeth becoming visible at approximately 17, 11, 5 and 4 days prior to parturition, respectively.^{36,97} (See pages 32, 33.) Fetal death late in gestation or at parturition can be diagnosed if the radiographs show the following: (1) alteration of fetal skull bone alignment: overriding of the fetal skull plate bones or extreme deformity of the fetal skull; (2) intra-fetal or perifetal gas collections; (3) abnormal fetal posture, "ball sign" or increased fetal flexion or straightening of the hind limbs.⁹⁷

The endocrine patterns have been studied for the pregnant bitch but not to quite the extent of those at estrus (Chart VI).²⁷ The sex steroid hormones, estradiol-17B and progesterone are similar in the nonpregnant and pregnant bitch up to the time of implantation (18 to 19 days post LH surge). Secondary elevations in proges-

terone levels are seen in the fourth and fifth week of pregnancy. This difference over the nonpregnant bitch cannot be used diagnostically because of the great individual variations encountered. Whether the increased progesterone is caused by increased luteal progesterone secretion or by placental gonadotropic activity is unknown at this time. Hemodilution that probably accompanies the rather dramatic anemia of pregnancy in the bitch from implantation to the end of gestation, probably effects the concentration of hormones, and if corrected, the higher progesterone levels of pregnancy versus nonpregnancy may be significant. The mean hematocrit (PCV) falls below 40% following implantation and by the end of gestation reaches 30 to 35 percent.^{27,35}

Serum estrogen levels rise during the latter third of pregnancy but do not reach levels as high as those observed during proestrus. Follicle stimulating hormone (FSH) increase in pregnant bitches has also been reported following implantation. The two-fold increase in FSH was observed as early as 28 days of pregnancy and was present to one week prepartum. This may account for the increased ovarian follicular activity and increased

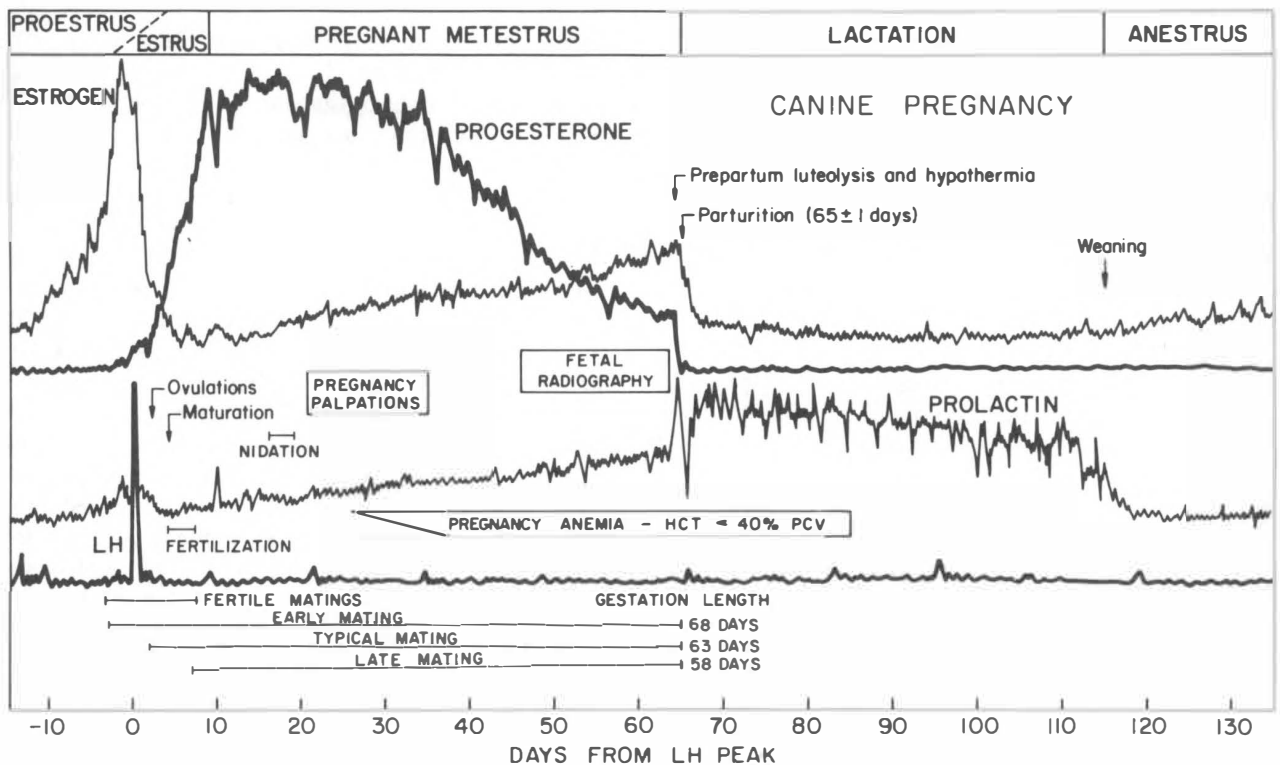


Chart VI. A schematic representation of typical endocrine changes reported, or presumed to occur, during the course of a fertile canine ovarian cycle including pregnancy and lactation, and their relation to events critical to breeding protocols, pregnancy diagnosis and estimation of gestation length.

(Courtesy and with permission of P. W. Concannon and publisher, W. D. Saunders, Co.²⁷)

estrogen levels in the second half of pregnancy.²⁷

Luteal progesterone is needed to maintain pregnancy in the bitch. This has been substantiated by several researchers. Removal of ovaries, hypophysectomies causing loss of LH and prolactin support of the corpora lutea, anti LH serum, suppression of prolactin with bromocryptine, prostaglandin F2a induced luteolysis in the last 30 days of pregnancy, all cause reduced serum progesterone levels to baseline and abortion.^{3,27,112,126}

Progesterone levels begin to drop between 30 to 35 days and 60 days of pregnancy from peak levels of 15 to 80 ng/ml to a prepartum plateau of 4 to 16 ng/ml, which is maintained for one or two weeks prior to parturition. Formation, full development, and progressive retrogression of the corpora lutea in the dog have been fully described and each phase occupies approximately one-third of pregnancy (0–21, 22–43, and 44–63 days postcoitum).³ The corpora lutea decrease in size after 37 days of pregnancy, but not until after 45 days is there histologic evidence of retrogression. Retrogression is progressive and remnants of corpora lutea can be detected for 2 or 3 subsequent estrous cycles.^{3,62} In non-bred bitches, degenerative signs are seen about the same time (42 days) as pregnant corpora lutea, but retrogression becomes more extensive at this time than in the pregnant bitch. By 5 to 6 months after the onset of estrus, corpora lutea in both bred and non-bred bitches are approximately 2 mm in size, are located deeper in the medulla of the ovary and have similar histological features.³

A pregnant specific two to five fold increase in serum prolactin (50 ng/ml) takes place with a rapid decline in progesterone the last few prepartum days.^{27,30,40} Prolactin levels remain high during lactation because of the suckling stimulus and decline to basal levels following weaning. Levels fall rapidly in bitches not nursing pups. In one study, PRL increased very rapidly during the 16 to 56 hours prepartum and reached peak levels (117 ± 24 ng/ml) at 8–32 (21 ± 3) hours prepartum in 6 bitches and at 24 hours postpartum in one bitch. By 36 hours after this peak, PRL levels were reduced to 37 ± 8 ng/ml before again increasing in response to suckling. Mean PRL levels increased during the first week of lactation, peaked at 86 ± 19 ng/ml at 1.5 weeks of lactation, fell slowly to 43 ± 6 ng/ml at 5 weeks, shortly before weaning, and then fell abruptly to 13 ± 2 ng/ml following weaning (Chart VI).³⁰

In the week prior to parturition maternal cortisol levels increase and are considerably increased 24 hours prepartum at the time that progesterone levels are falling. Concannon, et al. reported that on Days –3, –2, –1, 0 and 1 from parturition, mean plasma progestins were 4.2,

4.3, 1.6, 0.9, and 0.8 (± 0.2) ng/ml while the mean corticoids were 19, 19, 37, 15, and 14 (± 3) ng/ml.³⁵ In another study, mean serum progestin levels at approximately 120, 36, 20 and 10 h prepartum were 4.5 ± 0.6 , 3.1 ± 0.4 , 1.2 ± 0.4 , and 0.6 ± 0.1 ng/ml respectively. In 6 of 7 bitches, serum cortisol was elevated above mean prepartum levels of 23 ± 1 ng/ml during the day prior to the start of parturition, reached peak levels of 63 ± 7 ng/ml at 8–24 hours prepartum and fell to 19 ± 4 ng/ml at 8–12 hours postpartum. Mean serum cortisol levels remained between 22 ± 1 and 27 ± 5 ng/ml during lactation and weaning.³⁰ Dexamethasone treatment (2×5 mg daily for 10 days) from Day 30 of pregnancy caused, fetal death and fetal resorption, while treatment about Day 45 caused abortion or birth of dead fetuses at Days 55–59. A very accelerated decline of serum progesterone occurred after treatment in midpregnancy.⁶

By recording rectal temperature twice daily a transient hypothermia will parallel the decline in serum progesterone prior to parturition with a delay of approximately 12 hours. Rectal temperature falls about one to two degrees centigrade between 12 and 36 hours prepartum. During or following parturition, a rise in rectal temperature to slightly above normal takes place which will persist for several days.^{27,35} Further studies have shown that administration of prostaglandins F2 α (60 ug/kg divided bid or tid) can cause luteolysis, serum progesterone levels to fall rapidly, and some abortions in the last half of pregnancy. Rectal temperature also dropped within 15 minutes of PGF2 α administration, but only in luteal phase bitches and not in ovariectomized bitches, which suggested that the temperature drop depends on rapid drop in progesterone levels.^{32,35} Three bitches in this study did not abort, because progesterone levels remained at 2.1 ng/ml and after treatment of PGF2 α was stopped, progesterone levels returned to 5–10 ng/ml until normal prepartum decline. Progesterone serum levels must drop to baseline for parturition to take place. Exogenous progesterone given prior to Day 60 caused prolonged gestation, with either death of pups and the bitch if caesarian sections were not done.³⁵ What role prostaglandins play in natural luteolysis and parturition are not known. It has been shown that the canine pregnant uterus does produce PGE2 and PGI2 but no PGF2 α . Thus the PGE2; PGF2 α ratio may present a protective mechanism as it does in other species for the corpora lutea and maintenance of myometrial vascular tone during late pregnancy. Possibly PGF2 α is increased at the very end of gestation.^{27,83}

Parturition—The bitch at parturition is responsive to exogenous oxytocin, but measurements of endogenous

oxytocin have not been reported. Clinically the bitch appears like other species, that the neural reflex release of oxytocin occurs in response to cervical and vaginal distention during delivery of pups, digital "feathering" or stroking of the vaginal wall and suckling during lactation. The relaxation and dilation is probably caused by progesterone decline and estrogen increase at this time. The sharp prepartum prolactin rise may play a role in the anxiety, panting, scratching, chewing, nesting behavior, milk secretion, and seclusion that are usually observed 12 to 24 hours prior to whelping. It may also be responsible for other maternal activities such as removal of fetal membranes from pups, separation of the umbilical cord, eating of the placenta and licking and cleaning each pup as it is born. These same maternal behavioral signs and lactation may be seen in bitches with overt pseudopregnancy. (See pages 107-110.)

It appears that relaxin or a relaxin-like hormone is also present in the bitch, since along with increased estrogens the bitch shows great relaxation and softening of the sacroscopic ligaments, pubic symphysis, relaxation and dilatation of the vulva, vestibule and vagina.

The sequence of parturition in the bitch includes the three recognizable stages of labor. The first stage involves the anxiety, restlessness, nesting behavior, anorexia, seeking seclusion, and temperature drop of 1-2°C, 12 to 36 hours prior to whelping. The pelvic ligaments are softened with the tail head and tuber ischii becoming more prominent and the vulva lengthened, becoming flaccid and moist. Mild uterine contractions during this time can cause some of the restlessness. The second stage of labor is the true delivery of the pup or pups with usually one or two delivered at a time period and may consist of tenesmus and a few forceful strains similar to defecation resulting in the delivery of a pup in the non-complicated case. Over half are delivered in the anterior dorsal position, 40% in the posterior position. Usually extremities are extended, but birth in many can take place with a retained limb. Most bitches will deliver one or two pups every 30 minutes to 2 or 3 hours with the interval usually the longest following the first pup or pups delivered. Most bitches deliver their litter in 3 to 6 hours but can take up to 24 hours. Placentas are usually passed between the delivery of one or two pups since pups usually come alternately from each uterine horn. The third stage of labor, delivery of the placenta, is blended with the second stage. Most bitches will ingest the fetal membranes.

Suppression of estrus or control of estrus, contraception or complete sterility in the bitch are subjects of great interest and research in recent years. Different populations of dogs need different forms of control. The

most difficult group is the control of the stray, ownerless or homeless dogs (and cats) which require permanent sterilization of both sexes, instead of suppression or reversible control of fertility. These are usually dogs (and cats) owned originally by irresponsible persons. Animal shelters would like to provide sterile male and female pups, (kittens) or adults with a minimum of expense. A method or methods are needed that are effective, humane, permanent with one application, easily obtained by consumers, and easily provided by the health delivery system involved. Several studies and conferences have been held to provide measures to meet these needs, such as the National Conference on Dog and Cat Control, held in 1976 and sponsored by the American Humane Association, American Kennel Club, AVMA, Humane Society of the U.S. and Pet Food Institute.⁸¹ Several state and local societies have also studied the problem. A large part of their studies have been organizational, defining who is responsible, educational and informative to the public, setting control measures and the most difficult, finding finances for research and field trials to conduct studies on control of fertility or permanent sterilization.

Studies on the pet population in the United States are interesting and appalling. In nearly two decades of effort to raise public awareness and to educate conscientious pet owners, there appears to be little improvement.⁶¹ A report by APHIS-USDA in 1981 showed that 20 million dogs and cats are annually not wanted; 5 million are abandoned and 15 million are given to animal pounds and shelters.⁸⁰ Of those, 2 million are adopted and 13 million are destroyed. Faulkner's paper on pet population problems claimed that in 1973, 4.5 billion dollars were spent on combined care and feeding of pets, 18 million neglected pets were impounded costing society nearly 125 million dollars. To maintain a zero growth in the population, 72,000 dogs and cats must be destroyed each day. He also brought out the public health hazards, zoonotic diseases, waste problems of feces in highly populated areas and the trauma and fear of bites and stray dog packs.⁴⁹

Two studies in pet population control in a midwest U.S.A. college town showed that the dog population stayed stationary from 1968 to 1979 with 66% of all bitches spayed; with a people to dog ratio of 4.14:1 and a 12% population of roaming dogs with 36% of them, actually stray dogs. The cat population though was increasing by 18% annually. Only 59% of the females were spayed and it was calculated that 88% should be spayed to obtain zero population growth. The people to cat ratio was 5.2:1, household average was 0.508; 28% of all households had cats with 1.74 cats per household, whereas 43% of the households had dogs with 1.36 dogs per

household.⁷⁸ An excellent study by Schneider on the pet population in two areas of California from 1970 to 1975 showed an increase in pet owners, a reduction in the numbers of unwanted pets, increased life expectancies of pets and increased neutering of pets.⁹⁹

The only procedure available to the humane shelters is the spay or castration clinics which are expensive and time consuming. However, Faulkner stated that surgical sterilization or any alternative contraceptive technology deals with the consequence of the problem and not with its cause, which are irresponsible owners and inadequate control of irresponsible ownership.⁴⁹ Other methods currently being investigated are immunological control, especially with gonadotrophins, gonadotrophic releasing hormones, the ova, zona pellucida, fertilized eggs, spermatozoa, testicular tissue; the destruction of specific cells of the pituitary or hypothalamic area with cytotoxic substances, the formation of acyclic pets by testosterone sensitization of the perinatal hypothalamus and quicker methods of sterilization, utilizing laparoscopic techniques, electrocautery, lasers and injection of sclerotic or caustic agents for castration.^{1,13,28,48,50,59,72,73,92,104,138}

Probably no one method will answer all needs. Population control of other wild carnivores; coyotes and foxes are being studied for possible control of the stray dog. The second population of dogs to provide estrus control are those that are owned by conscientious persons that want to produce litters, but need estrus suppression or control to avoid the nuisance of estrus while using the bitch for performance, show, work and also to avoid the problem of confinement, attraction of males and possible unwanted pregnancies. When unwanted breedings do take place, then mismating, "day after" or pregnancy termination methods are needed.

Options for preventing estrous cycles or pregnancy in the bitch still remain limited to veterinary practitioners in the United States compared to other countries in the world. If permanent sterility is desired, then the best method available is ovariectomy. This is not without postoperative complications. In one study of 109 bitches, referred to a University clinic over a 30 month period, 28 bitches had a persistent vulvar discharge, 37 attracted male dogs, 28 showed periods of estrus, 14 had postoperative pseudopregnancy. Pseudopregnancy may occur post surgically when bitches are spayed in the luteal phase causing a rapid fall in blood progesterone levels and a release of prolactin which may simulate the same hormone sequence as parturition.²⁷ Forty seven of these bitches had remnants of ovaries left on exploratory surgery (41 right side, 22 left side); 70% had elevated progesterone levels, 39% had cyclic vaginal smears; 19 bitches had uterine stumps infected and inflamed.^{81a} One

case report involved a bitch with a partial hysterectomy; ovarian cycles continued; three years post surgery a vaginal discharge was discovered and on surgery the remaining uterus and cervix contained abscesses and granulomas from which *B. canis* was recovered. A high *B. canis* titer was maintained for at least one year after removal of ovaries, remaining uterus and cervix and therapy with tetracycline.^{40a} These reports indicate that good techniques are required and that complete ovariohysterectomies are much preferred over tubal ligations, ovariectomy, salpingectomies or subtotal hysterectomy which frequently lead to uterine, cervical and/or ovarian disease. There is a move to encourage spaying prepubertal or pubertal bitches for several reasons; the infantile tract is located and removed with minimal time and trauma. There is little or no chance of developing mammary gland tumors and there is no chance of several unwanted litters before accomplishing ovariohysterectomy. Post complications of prepubertal spayings may result in a higher incidence of juvenile vulvas, perivulval dermatitis and hypoenestrogenism with bilateral miliary dermatoses. Increased obesity may be seen in some bitches, but frequently the young bitch will have a greater tendency to exercise well and exercise and diet control will control the obesity problem. To what extent bone development, epiphyseal closure, or adult body conformation will change is not known and further studies are needed.²⁸

For control of estrus, reversible contraception by pharmacologic means is available with synthetic progestins or androgens.^{16,28,135} One of each for use in the dog are approved for use in the United States ("Ovaban," Schering Corp, Kenilworth, N.J. and "Cheques," Upjohn Co, Kalamazoo, Mich.). With either of these two steroids, estrus can be prevented and pregnancies postponed. Manufacturers recommendations should be followed. They are not the answer for life control for estrus nor are they meant to replace ovariohysterectomy. They are products to be used in young bitches prior to uterine or ovarian disease. Bitches that were not planned to be bred or have finished their reproductive use should be neutered.

Megestrol acetate ("Ovaban") is marketed in the United States as a canine contraceptive in 5 and 20 mg tablets for oral use. It is distributed as "Ovarid," Glaxovet Ltd., Greenford, Middlesex, in the United Kingdom and Europe. It is a potent oral progestin with a very short half life, with total elimination from the bitch in about 8 days.¹⁶ It can be administered at two times of the cycle to control estrus, either in anestrus or the first 3 days of proestrus. The recommended dose for anestrus bitches is 0.25 mg/lb (0.55 mg/kg) body weight for 32 days. The time for anestrus treatment must be selected on the basis of

the bitches' history of interestrous intervals and be at least one or two weeks prior to the next expected proestrus. The return to estrus averages 4–6 months (1–7 mo. range).

The proestrus dose is 1 mg/lb (2.2 mg/kg) for 8 days, which is the same total dose for the 32 day treatment. The occurrence of proestrus should be verified by examination of vaginal cytology. The bitch should be confined for 3–8 days or until cessation of bleeding and loss of attraction for males. Usually proestrus subsides in 3 to 8 days. Again, most bitches return to estrus in 4 to 6 months (1–7 mo. range). If treatment is started too early in proestrus, the bitch may return to proestrus, if too late in proestrus, a fertile estrus may occur.²⁸

British work on "Ovarid" reported that return to estrus can be delayed by administering megestrol acetate at 1 mg/lb, (2.2 mg/kg) for 4 days, beginning during the first 3 days of proestrus, followed by 0.25 mg/per lb (0.55 mg/kg) for 16 days which again is the same total dosage as the other two regimes. They also recommend that if mating occurs during the first three days of treatment, megestrol acetate therapy should be stopped and the bitch treated for mismating. If mating occurs after 3 days of treatment, therapy should be continued at 3 to 4 mg/kg since the drug will prevent pregnancy in most cases. British work also prescribed megestrol acetate for up to 4 months following a postponement course of therapy for extended suppression, but these bitches should be allowed a normal cycle before being retreated.¹⁶

Precautions indicated by the manufacturer for "Ovaban" are; not to administer for more than 2 consecutive treatment periods; do not use in bitches with reproductive tract disease, pregnant bitches, or bitches with mammary tumors; do not use in first estrus or pubertal dogs. A report has shown that it is safe and effective in first-heat or pubertal bitches when the onset of proestrus is accurately determined and treatment administered as prescribed for proestrus.⁹ Clinical trials reveal suppression of estrus in 92% of 387 bitches in early proestrus and 97% of 117 in anestrus with minimal adverse effects.¹⁷ Treatment did not affect subsequent cyclicity and fertility.

Temporary minor side effects include increased appetite, decrease of activity, calming effect, less aggressive behavior, weight gain, water retention and rarely lactation. Therapy during either the first or second half of pregnancy did not result in fetal abnormalities. Overdosage or prolonged therapy may cause cystic endometritis or Cushingoid syndrome.^{14,15,16,28}

"Mibolerone" is a synthetic androgen-derived steroid and is approved for long-term estrus prevention in dogs as "Cheque" drops to be added to food daily in the United

States and as "Matenon" in the United Kingdom. Approval has been obtained in the United States to market mibolerone in canned dog food as a prescription diet. It is androgenic, anabolic, antigonadotrophic and does not possess progestational or estrogenic activity. Inhibition of estrus was over 95% successful in dogs treated for periods up to 5 years and possibly it may prove capable for life-time use.^{16,111} Manufacturers recommended treatment for up to 2 years, starting in early or mid anestrus. Treatment should start at least 30 days prior to the onset of the next proestrus to completely suppress estrus. It will not arrest proestrus or estrus like megestrol acetate, and will not interfere with conception or gestation, however, female puppies were masculinized.^{16,110,113}

Dosage ranged from 30 µg/day for dogs weighing 1 to 12 kg. up to 180 µg/day for dogs over 45 lbs, German Shepherd Dogs and any German Shepherd cross-breed which for unknown reasons require the high dosage. Undesirable side effects include: mild clitoral hypertrophy which is worse in prepubertal bitches to the point of os penis formation; vaginal or vulval discharge, especially in those with an enlarged clitoris; masculinized deeper voice, masculinized hair coat, especially over the neck region; anabolic effects; overdose leads to anal gland inspissation and resulting odor; increase severity of preexisting seborrheic dermatitis; and occasional elevation of liver function test which returns to normal when the compound is removed from the diet.^{16,28,111}

Bitches that show estrus while on therapy are either receiving too low a dose, started with less than 30 days to estrus, or therapy was not reliably administered. Return to estrus following cessation of administration is usually 2 to 3 months but may be as short as 7 days and up to 7 months.^{16,28} Bitches that are on higher doses than recommended may also have a decrease in the post treatment size of the first litter.¹¹¹

Several other non-approved steroid hormones have been shown to suppress or inhibit normal ovarian cyclicity in the bitch. Excellent reviews on their use and side effects have been reported.^{16,28,60,103} The steroids used include natural steroids, progesterone and testosterone, and synthetic steroids including medroxyprogesterone acetate, melengestrol acetate, proligestone, norethisterone acetate. It is felt that all of these work by mimicking the normal feedback effects of endogenous ovarian steroids or in the case of androgens, testicular steroids, on the hypothalamus (releasing hormone and/or pituitary gonadotrophins, FSH and LH). All of the above steroids are effective in controlling ovarian cycles in the bitch, but have undesirable side effects: progestins promote uterine disease, mammary gland hyperplasia, and other effects on pituitary and adrenal cortical functions, whereas

androgens have masculinizing effects. Both progestins and androgens can cause fetal reproductive abnormalities if given during pregnancy.^{39,132}

Medroxyprogesterone acetate, MAP or also known as α -methyl 17 α acetoxy progesterone, MPA ("Promone," Upjohn) was marketed as an injectable canine contraceptive in the U.S. until 1969. It was removed at that time because of the high incidence of cystic endometrial hyperplasia, endometritis and pyometra.^{4,11} This effect may be related to overdosing or administering during stages of the cycle other than anestrus since the importance of a synergism between progesterone and estrogen to cause increased uterine disease was confirmed earlier.¹⁰³ High doses of MAP (MPA) also cause mammary gland tumors, adrenal suppression and acromegaly.^{29,45,101} With reduced amounts, (50 mg/dog) estrus was prevented and normal fertility followed,¹² but later studies using this dose, either single or multiple injection schedules, caused uterine disease.¹⁰³ However MAP/MPA is still used widely in other countries as a contraceptive ("Depopromone," "Perlutex," "Anovulin") and is marketed in the U.S. for human use other than contraception as "Depo-Provera" (Upjohn Co.) The minimal effective contraceptive dose is approximately 2 mg/kg every 3 months.

Melengestrol acetate, MGA, another progesterone, effectively prevented estrus in dogs at 200 μ g/day, but levels of 4 or 8 μ g/kg produced abnormal uterine changes, dystocia and pyometra.^{52,114}

Proligestone (14 α 17 α propylidene-dioxyprogesterone), a progestin, is an injectable canine contraceptive marketed in Europe as "Delvosterone" (Mycofarms, Ltd. and Gist-Brookades).¹³¹ Doses of 10 to 30 mg/kg depending on the weight of animals, are injected subcutaneously at zero, three and four months followed by others at 5 month intervals thereafter. Administration during proestrus resulted in signs disappearing within 5 days and retreatment of these animals within 3 months resulted in continuing persistence of anestrus in 97% of animals treated. Clinical trials showed no formation of mammary gland tumors, only 0.3% of uterine disease and none of these were in proestrus treated cases (1685 cases). There appears to be little or no restrictions on usage at any stage of the cycle.^{28,103,131}

Silastic implants containing 169 μ g/kg of testosterone controlled estrus for as long as 840 days with normal estrus cycles and litters after removal.¹⁰⁵ Androstenedione, at a dose of 400 μ g/day/dog was not effective in preventing estrus. No uterine disease was observed, but mammary gland development with milk secretion (4/13), clitoral enlargement of all treated and one pregnant bitch with testosterone implants in situ produced two female pseudohermaphrodites.

Progesterone implants placed subcutaneously in bitches inhibited cycles for 15 to 20 months with no objectionable side effects. These implants, although effective, will probably not be made available commercially because they are not biodegradable and must be inserted and removed surgically.²⁸

A 19-norandrogen, norethisterone called "Norlutin A" (Parke Davis) was used orally to suppress estrus in Greyhound bitches. A 4 week treatment regime starting at proestrus delayed the return of estrus for 132.9 days average. Four bitches had normal litters following treatment.¹⁰³

A synthetic 19 norsteroid, 6,6, spiroethylene, 19-nor-estrioxenone, effectively suppressed the occurrence of estrus in dogs when administered orally once daily for 90 days at a dosage of 0.9 mg/kg body weight. There was no evidence of mammary gland or uterine disease during the period of treatment.⁷⁶

Testosterone propionate has been used to prevent estrus, especially in racing Greyhounds, for up to 5 years at an oral dosage of 25 mg per week. Many of these have returned to normal reproductive status. Clitoral hypertrophy and vaginitis are frequent side effects with clitoral hypertrophy being so prominent in some Greyhound bitches that they are referred to as "tail-lighters."¹⁶ Other side effects such as premature epiphyseal closure if immature bitches are treated and urogenital anomalies, hermaphroditism in female pups born to treated pregnant bitches, makes testosterone objectionable.

The oral administration of 2 to 4 drops of a 1% solution of pilocarpine has been reported to suppress estrus in bitches, but the action and method of control has not been reported or investigated.^{16,28}

Vaginal devices ("Option I") have been marketed and used as a contraceptive but since have been discontinued because of expense, various sizes needed, problems with fitting, poor retention, vaginal discharges, rejection and loss, unacceptable failure rates and dissatisfaction on the part of owners and veterinarians.

Immunization as described for population control and use in either bitches or studs may have value for temporary estrus suppression and control of spermatogenesis through LH or GnRH control, but a great deal of research is needed to find the right antigens, protocols for repeatability of effect, evidence of any deleterious effects and overcome the disadvantage of the need for irritating adjuvants for antibody production.

Luteinizing hormone, LH, given during proestrus has been reported as a possible antifertility drug for that cycle (20 units/kg-IV). This is repeated once again 2-3 days after the first injection if proestrus has not subsided. The effect is supposed to cause premature luteinization of follicles instead of stimulating further follicular growth

and maturation. The effect would depend on timing of administration so that follicles are young enough to ensure premature luteinization and not ovulation. This would be similar to reports of premature luteinization of follicles when too early attempts are made to induce estrus in bitches using PMSG or FSH and following with LH or HCG resulting in preovulatory luteinization instead of ovulation.²⁸

For years estrogens have been used as post-breeding, "day after," misalliance and antinidatory treatment in bitches that were mismated. A variety of estrogens have been used with little scientific and experimental evidence of their effectiveness and side effects. Diethylstilbesterol, before it was removed from use in the United States, was the hormone of choice and continues to be used in many countries where it is still legal. Since then, several of the longer acting available estrogens are being used, especially estradiol cypionate (ECP) followed by estradiol valerate or benzoate and finally estrone. Few statistics are quoted for their success and/or for failure. One report revealed, that 1–2 mg of ECP given intramuscularly the first 5 days following mating had prevented conception in 537 consecutive cases.⁶⁵ Several failures had resulted when ECP was given later than 5 days after mating. It was indicated that these animals should receive a second injection of ECP five days after the first or receive oral diethylstilbesterol tablets at the rate of 1 to 2 mg daily for five days. Estrogens usually delay the transit of zygotes in the oviduct and may affect the development of zygotes directly (zygototoxic).¹⁰³

Holst and Phemister have shown that oocytes remain in the oviduct until one to three days after the vaginal smear is no longer fully cornified or the beginning of metestrus/diestrus.^{55,56} Since a bitch can accept a male over a long period of time, late proestrus to early metestrus/diestrus, it is very important that vaginal smears be made and the cytology studied for stage of cycle when the bitch had coitus and judge the most appropriate time for "mismating" with estrogen therapy. Concannon has given excellent guidelines on the use of ECP until more scientific evidence is presented for its use in misalliance. If the smear is still of estrous type, only a most conservative dose of ECP should be considered (0.1 mg/10 lbs, max. of 0.5 mg); if the smear is not fully cornified or late proestrus, a delay of 1 to 3 days before estrogen administration should be considered because the bitch probably has not ovulated. Remember, semen in the uterus can be fertile for 5–6 days or possibly to 11 days or at least until metestrus.⁴¹ If the vaginal smear is very late estrus or early metestrus, then an intermediate or less conservative dose can be given (0.2 mg/lb for a total of 1.0 mg). These doses are based on clinical impressions and published reports.^{28,58} Estrogen will lengthen the es-

trus or attractiveness and if given in proestrus may do little but delay the LH surge and the bitch eventually reaches estrus and may become pregnant. Bitches must be confined during this prolonged acceptance period. Bitches that have received the long acting estrogens are more prone to developing pyometra in 2 to 6 weeks, which is frequently an "open" pyometra with a mucopurulent or mucosanguinous vulval discharge. Excessive estrogens can cause aplastic anemia, thrombocytopenia and a hemorrhagic syndrome with a rapid course and death.^{10,66} Concannon has reported on the several forms of estrogens used for mismating bitches with no scientific data on safety, side effects or effectiveness (Chart VII).²⁸

An antiestrogenic compound, 3-4-trans-2,2-dimethyl-3-phenyl-3-4-p-(B-pyrolidinoethoxy)-phenyl-7-methoxychroman, devoid of progestational, androgenic, or antiandrogenic activity, was reported to be effective when given 24 hours after mating to prevent pregnancy. It can be given orally or parentally in a single dose to interfere with ovum development.¹⁰³

Administration of two compounds, (L10492) and (L10503) prevented pregnancy in bitches most effectively when administered at 20 days postbreeding, about the time of nidation. A single dose of 100–150 mg/kg was administered. When given at 45–48 days, they caused resorption in 2 bitches and expulsion of macerated fetuses 1 week past the due date. Undesirable side effects include loss of appetite and diarrhea for 3–8 days beginning 1–3 days after the start of treatment.¹⁰³ These drugs seem to work on the utero-placental complex directly and do not influence pituitary or ovarian function since plasma progesterone levels remain normal post treatment.

Termination of pregnancy after diagnosis has also become an alternative choice after an undesirable mating. Several drugs have been used including estrogen implants, prostaglandins, bromoergocryptine (an ergot alkaloid) and dexamethasone.

At midpregnancy, silastic capsules containing crystalline estradiol, sufficient to maintain blood levels of estradiol of proestrous level, were inserted subcutaneously. All bitches treated either resorbed or aborted their litters.²⁸

Adrenal corticosteroids have the potential to terminate established pregnancies in the bitch. One study reported on the use of dexamethasone at 5 mg twice a day for 10 days with intrauterine death and resorption when started at 30 days; and birth of dead fetuses at days 55 to 59 when treatment started at day 45.⁶

Bromoergocryptine, an ergot alkaloid, reduces prolactin secretion as a dopamine agonist, is luteolytic and when administered to bitches at 0.1 mg/kg/day for 6–10 days

Dosage (per bitch)	Comment	Reference
<i>Repositol Stilbestrol (DES)</i>		
0.4 mg/kg	Within 36 to 48 hours	Mann, 1971
1.0 mg/kg	Safety questioned	Jochle, 1975
1.1 mg/kg	Within 5 days	Merck Veterinary Manual, 5th ed., 1980
2.0 mg/kg	Maximum dosage 25 mg	Jackson and Johnston, 1980
<i>Estradiol Cypionate (ECP)</i>		
0.25 mg/30 kg	Maximum dosage 0.5 mg	Okin et al., 1976
0.125 to 1.0 mg		Jackson and Johnson, 1980
0.25 mg	For toy breeds	Merck Veterinary Manual, 5th ed., 1980
0.5 to 2.0 mg	Within 5 days	Merck Veterinary Manual, 5th ed., 1980
1.0 to 2.0 mg	Within 5 days	Jochle, 1975
1.0 to 2.0 mg	If after 5 days	Jochle, 1975
<i>Estradiol Valerate</i>		
3.0 to 7.0 mg	Once, days 4 to 10	Jochle, 1975
<i>Estradiol Benzoate</i>		
0.5 to 3.0 mg every other day	Three injections, days 4 to 10	Jochle, 1975
<i>Estrone</i>		
2.0 to 5.0 mg	Within 5 days	Okin et al., 1976

Chart VII. Antinidatory Injectable Estrogen Treatments Indicated for Mismatched Bitches Without Data on Safety or Side Effects. Refs. (1) Mann, 1971; (2) Jochle, 1975; (3) The Merck Veterinary Manual, 5th ed., 1980; (4) Jackson and Johnston, 1980; (5) Okin et al., 1976. (Courtesy and with permission of P. W. Concannon and publisher, W. D. Saunders, Co.²⁸)

it terminated pregnancy in 60% of bitches studied. Nausea, depression, anorexia are some of the deleterious side effects reported.²⁷

Prostaglandins of the F series, PGF_{2a} are used in the bitch for their luteolytic and smooth muscle effect, resulting in cervical dilatation and uterine contraction. This effect causes luteolysis and abortion in midpregnancy; approximately from 30 days to parturition in the bitch. The current popular clinical use of PGF_{2a} is to treat pyometra—endometritis in the bitch and queen. Prostaglandin analogues have also been studied in the bitch to cause luteolysis and abortion. The right analogue could become a very important drug for small animal use because they usually are much more potent and long acting with lower dosage, and less side reactions.

The median subcutaneous lethal dosage for PGF_{2a} in the bitch was determined to be 5.13 mg/kg.¹¹² Clinical signs of side reactions and toxicosis include excessive salivation, vomiting, diarrhea, hypernea, ataxia, urination, anxiety, and pupillary dilatation, then constriction. Severity of side effects are dose dependent. At low dosages, defecation is more frequent, while at intermediate dosages, hypernea, anxiety, hypersalivation, vomiting and defecation have been observed. Higher doses have

caused ataxia and slight depression.⁹⁰ The clinical dose range in the bitch has been from 0.02 to 1.0 mg/kg or 20 ug to 1000 ug/kg administered usually intramuscular or subcutaneously.^{32,90}

Side reactions are seen in 20 to 120 minutes post injection. Death in animals given lethal doses range from 2 to 12 hours post injection.¹¹² Bitches seem to adapt to PGF_{2a} with side effects diminishing by the fourth or fifth treatment. Prostaglandin F_{2a} or analogues should not be used in dogs with asthma, liver, kidney or cardiac problems.

Early researchers thought that PGF_{2a} was not luteolytic in the dog but did cause temporary lowering of serum progesterone levels for a brief time.^{3,7,63} Concannon was the first to show that 20 ug/kg every 8 hours or 30 ug/kg every 12 hours for 3 days caused abortion in 4 of 7 bitches started on treatment on days 33 to 53 of gestation, with abortion occurring 56 to 80 hours after initial treatment.³² Progesterone plasma levels were 0.6 to 1.4 ng/ml when abortion occurred. The 3 bitches that did not abort had a mean low value of 2.1 ng/ml of plasma progesterone during PGF_{2a} treatment beginning on day 31 to 40 of gestation. Their plasma progesterone recovered to 5–10 ng/ml and were maintained until nor-

mal prepartum decline. In this study, 8 nonpregnant bitches in mid or late luteal phase were also treated and all 8 had complete luteolysis with low anestrus baseline plasma progesterone levels afterwards. Two nonpregnant bitches in early luteal phase (days 5 and 20) were also treated and plasma progesterone levels were not drastically altered.

Concannon also found a transient fall in rectal temperature within 15 minutes and maximal at 45–60 minutes postinoculation that averaged 1.39 °C. No change in temperature was seen in ovariectomized bitches treated with PGF_{2a}. It was concluded that hypothermia was due to the 20 to 45 percent fall in plasma progesterone levels within the 15 minute period postinoculation of PGF_{2a}.

Ten mated bitches were given 250 ug/kg of PGF_{2a} bid; 5 between the first and fifth days of metestrus and 5 between 31 and 35 days of metestrus.⁹⁰ Early metestrus dogs were not affected and appeared the same as the 5 nontreated controls, whereas all 5 in midgestation had complete luteolysis, hypothermia following the initial injection of PGF_{2a} and abortion following the fourth to eighth injection.

Prostaglandin analogues, fluprostenol and cloprostenol ("Equimate" and "Estrumate," respectively, Imperial Chemical Industries, U.K.) were administered to 42 Beagle bitches at gestational periods of 4 to 35 days at doses from 10–40 ug/kg.⁵⁷ A slow releasing formula of both analogues (48 to 72 hours) and a 24 hour release intravaginal device of both analogues showed minimal acceptable side effects compared to the aqueous marketed form of cloprostenol. Sustained depression of plasma progesterone levels and pregnancy termination were seen in 6 of 22 bitches (27%) treated before day 25 of gestation and 16 of 20 bitches (80%) treated on or after day 25. An interesting effect was that 2 bitches whose pregnancies or corpora lutea were terminated at 14 days by the 40 ug/kg cloprostenol injection showed clinical estrus 10 to 14 days after treatment with normal mature ovarian follicles at necropsy. This suggests that a bitch could possibly be remated in a few weeks after correction of a misalliance in the first 2 weeks instead of having to wait until the next cycle at 4 to 12 months.

Eleven pregnant bitches were treated with a single subcutaneous injection of 20 ug/kg of synthetic prostaglandin analogue (TPT) in an aqueous buffer.¹³³ Five bitches treated between days 30–43 of pregnancy aborted 5.4 ± 1.4 days following treatment. Two of 4 bitches treated on days 20–22 of gestation continued to normal term, while the other 2 appeared to resorb their fetuses following diagnosis by palpation on day 28. Two others treated on day 9 had normal pregnancies.

Further work by this group utilized bitches on days 20–22 of pregnancy and administered TPT subcutane-

ously in different treatments: minipump at a rate of 10 ug per hour for either 24 or 48 hours, single injection of 200 ug in either aqueous, or polyethylene glycol 400 or the methyl ester of TPT in polyethylene glycol 400.¹³⁴ All treatments caused abortion or resorption with the best treatments being those that had the longest administration of analogue; 48 hours minipump, 5/6 aborted and the methyl ester of TPT, 3/4 aborted.

Eight bitches were given 5 to 30 mg of PGF_{2a} on day 5–17 of pregnancy which resulted in a marked temporary decrease in progesterone levels and in those given 20 mg or more deaths occurred in some or all of the embryos after implantation. Seven bitches given 5–50 mg of PGF_{2a} in 25–51 days of pregnancy resulted in only one animal given 20 mg of PGF₂ having a premature birth at day 51. All others were normal. Bitches given 5–10 mg of PGF_{2a} on days 55–58 of pregnancy resulted in induced parturition in 38.1 hours. In this study, side effects of PGF_{2a} were intense in bitches given 10 mg or more of PGF_{2a} and those treated during pregnancy returned to estrus about 40 days earlier than untreated control bitches.¹³⁰

The above research indicates that the early corpora lutea are quite resistant to exogenous prostaglandin until midgestation, 25 to 30 days to term. The author has aborted 6 mismated bitches. Their ages ranged from 8 months to 5 years, gestations ranged from 31 to 60 days, and a range of 2 to 8.5 days of PGF_{2a} therapy was needed to cause abortion. Treatment consisted of 25 to 50 ug/kg of PGF_{2a} (Upjohn Co., Kalamazoo, MI) intramuscularly, given twice a day. The lower dose was given the first day or two to observe the severity of side effects and to relax the cervix. These bitches showed nesting signs 24–48 hours prior to abortion. Vaginoscopic examination of 3/6 bitches revealed daily changes in the anterior vagina with increasing edema of the vaginal and cervical folds, fluid, and dilation of the cervix 24 to 48 hours prior to abortion. The two late gestation bitches, 57 to 60 days of gestation, aborted at 2 and 4.5 days of treatment, respectively, and both had live pups. The bitch at 31 days of gestation aborted 3 pups 6 days post initial treatment and abortion appeared to be complete. She was given 10 i.u. of oxytocin intramuscular the following day to enhance uterine involution. Two weeks later, two retained viable fetuses were noted on palpation and radiographs. The bitch whelped 2 normal live pups and has had 3 normal litters since. All bitches returned to estrus at normal intervals. One bitch had prolonged postpartum hemorrhage for 6 weeks that was diagnosed as subinvolution of placental sites. All bitches showed varying individual slight side effects the first 15 to 60 minutes post injection including increased salivation, diarrhea, emesis, and panting.

The above work shows that $\text{PGF}_{2\alpha}$ can be used to cause abortion in healthy bitches from midgestation to term. A dose range of 25–250 $\mu\text{g}/\text{kg}$, given intramuscular, BID to effect can be used. Hospitalization and close observation are necessary and the later the stage of gestation the quicker the effect. More research is needed on the analogues, different routes of administration such as the intravaginal route, possible early gestation luteolysis and early return to estrus.

Induction of estrus and ovulation with successful breeding is desired at times for convenience of a timed whelping for companion dogs, show or performance bitches, research dogs, infertile bitches with a history of never expressing estrus or having an abnormal long interestrus period (usually >12 months). The infertile bitch with this history should have a physical and reproductive tract examination, thyroid function test for hypothyroidism, vaginal cytology and a blood serum progesterone test to determine true anestrus or a possible missed cycle.

Gonadotrophins, follicle stimulating hormone, (FSH), pregnant mare serum gonadotrophin, (PMSG), luteinizing hormone, (LH), and human chorionic gonadotrophin (HCG) and gonadotrophin releasing hormone, (GnRH), estrogens and some human fertility drugs have all been used, in different regimes, combinations and dosages with varying success. Several have induced estrus with or without ovulation, normal or degenerate ova, and few have been highly successful in producing normal pregnancies or having repeatable results. The induction of estrus in the queen is much more predictable than in the bitch.^{21,43,44,46,60,64,67,68,86,89,102,103,118,129,140,141}

The use of PMSG daily, utilizing either 250 IU/day, 500 IU/day or 20 IU/kg/day for 10 days with 500 IU of HCG combined on the last day of PMSG treatment resulted in successful induction of estrus and ovulation in 14/25 bitches.¹¹⁸ Another researcher, used these same regimes for 8 days, with successful induction of estrus and ovulation in 6/6 bitches.¹⁰³ The undesirability of causing premature luteinization of follicles with HCG is important to consider. The 10 day interval from the start of treatment is about the normal interval for follicular growth in the dog prior to the preovulatory LH surge.¹⁰³ Another group reported on the use of 20–50 IU/kg/day, IM for 9 days or 500 to 1000 IU/day, I.M., of PMSG, two treatments, six days apart, followed by either 500–1000 IU/day, I.M. on the first and second day of estrus or 2 treatments of GnRH, 50 μg , IM, each six hours apart on the first day of estrus. Bitches treated with these regimes ovulated 60% of the time. Ovulation was determined by serum progesterone increase or pregnancies following artificial insemination.^{19,21} This group found PMSG more effective than FSH-P. These treatments appear to work in the truly anestrus bitch and appear to

be more effective when administered intramuscular instead of subcutaneously. If the bitch is in metestrus/diestrus with progesterone levels above basal levels, then pretreatment with either estrone or estradiol is recommended. Pretreatment with 100 to 300 μg of estrone per day for 5 to 6 days produced vulval bleeding. This was followed by the regime of PMSG and HCG previously mentioned and resulted in normal pregnancies. Either PMSG or FSH-P if used indiscriminately can cause cystic follicular degeneration. Induced bitches should be bred every other day for three matings starting with the first day of acceptance. In another study, 4/8 bitches had fertilized ova or pregnancies when 200 IU of PMSG and 500 IU of HCG IM was followed by 500 IU of HCG 3 days after the vaginal smear was fully cornified.¹²⁹ Wright induced estrus in eleven anestrus bitches with 110 IU/kg of PMSG given once weekly until estrus occurred or until 3 treatments had been given. Estrus occurred in 8 of 11 bitches. Three of 8 received 500 IU of HCG on the first day of estrus resulting in 7/8 bitches ovulating with those receiving HCG having a better ovulation rate (88.6% vs 46.1%). In a later study, 8 anestrus bitches were given 250 IU of PMSG per day until estrus occurred, or till 20 days of treatment. Then 500 IU of HCG was given on the first day of estrus or on day 21. Six of 8 ovulated, 3 with 100% ovulation rates; two showed estrus at 14 days, the rest went to day 20.^{140,141} Several regimes using either PMSG and HCG, sheep pituitary gonadotrophin ("Vetrophin") or equine pituitary gonadotrophin ("Pitropin") are reported with about 85% normal dogs induced at the proper time and 65% of bitches with prolonged anestrus showing good standing estrus after treatment with expectation of normal conception and litter rates.⁴⁶

One FSH and LH scheme was reported to cause follicular growth but not ovulation.⁸⁹ Another method, utilized 1 mg diethylstilbesterol oral tablets daily for 4 days and on day 8 twice daily injections of 2 mg FSH subcutaneously, until the vaginal epithelium was 90% cornified (about 8 days of FSH) followed by 500 IU of HCG I.V. Most bitches accepted the male 48 to 72 hours post HCG. This regime has produced small litters in bitches with prolonged anestrus but not in normal anestrus bitches.⁸⁵ The author prefers a method of weekly 25 mg FSH injections, I.M., in truly anestrus bitches, until vulvar enlargement or a bloody vulval discharge occurs.⁶⁷ The author only gives FSH for up to 5 treatments. If estrus does not occur then one month's rest and repeat the regime for another five weekly treatments. Most bitches will show estrus after the second and third FSH injection. At each injection day, vaginal cytology is performed for evidence of increased estrogens and follicular development. Once proestrus is determined, then every

day vaginal cytology is taken and the bitch is bred at estrus every 48 hours for 3 or 4 times. If proestrus occurs but doesn't proceed to estrus by daily increasing superficial cells or cornified cells on daily vaginal smears then daily FSH injections starting with 25 mg on day 1, 10–15 mg on day 2 and 5 mg on day 3 will usually cause complete cornification and estrus. This bitch is then given 500–1000 IU of HCG, IM, when fully cornified and bred as described above. Approximately 60% of bitches treated in this manner will ovulate, conceive, have normal pregnancies and litters.

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Reproductive Physiology of the Queen

Puberty in queens usually occurs between 7 and 12 months of age depending upon their nutritive state, breed, freedom from disease and season of the year that they are born. Queens may have their first estrus as early as 4 months of age if they obtain the minimal body weight of 2.3 to 2.5 kg or they may be as late as 21 months of

age. If the normal pubertal age and weight are attained during the anestrus period of October to December, cycling usually begins in January or February following birth. If pubertal weight is attained in early or late summer then an early pubertal estrus may take place.⁴⁸ Males usually reach puberty at a minimal body weight of 3.5 kg which is attainable at 9 months of age. (See pages 409–411.)

Purebred cats may reach puberty later than non-purebred cats. Cats that are housebound versus a free-roaming environment, especially those that are housed without other cats, may reach puberty later.¹⁸ A British study of several breeds showed that puberty on the average was seen between 9–10 months of age, with considerable breed difference; Himalayans or colorpoints were the oldest, average 13 months (9–18 mo.), while Burmese were the youngest, average 7.7 months (4.5–15 mo). They noted that puberty was affected by age of kittens at weaning, time of year litter is born, natural or artificial increase of daylight and the breed of cat.³⁰

The reproductive life of the cat is long, with both toms and queens known to continue breeding for 14 or more years, with a period of 8 to 10 years most common for continuous breeding of a queen. (See page 110, 111) **Litter size** is reduced with age. Most queens will have two litters of 2 to 6 kittens with an average of 4 each per year. Some will produce 3 litters per year. Siamese cats or their crosses have slightly larger litters (average 6). First litters of pubertal breedings are usually small and rearing is less successful.^{34,38}

The estrous cycle—The queen is seasonably polyestrous, a long day breeder, similar to the mare.²⁹ Breeding season in temperate zones usually begins 20 to 60 days after the winter solstice and may end any time after the summer solstice. In the northern temperate zone, breeding usually begins in January or February and extends through the early part of September with a range of August to October or early November.^{18,22} The first cycle usually will occur between January and March, the second from April to early July, and the last during late July through early September.¹⁸ The author has frequently noted the first cycles of the year will be during a January or February thaw in free-ranging cats. Again, like the mare, kittens can be born in any month of the year.³⁰

In conditions of artificial light or combinations of natural and artificial light, where queens receive 12L:12D, 14L:10D, or 16L:8D, many will cycle throughout the year. Fourteen to 16 hours of light versus 12 hours will increase the percentage of cycles. Even in colonies with artificial light, some queens will experience a winter anestrus.²² Winter anestrus was reported

in 90% of long-haired cats (aver. 4 mo., 2–9 mo.) from September to January, whereas 60.8% of shorthairs remained cyclic throughout the year. More queens of all breeds confined indoors remained cyclic, while those allowed or confined outside, usually become anestrus.³⁰ Tom cats will show depressed sexual activity during the winter period.⁴⁸

The vomeronasal organ, which is a blind pouch dorsal to the hard palate and communicates with the nasal and oral cavities via the nasopalatine duct that opens behind the incisors, is thought to be used to perceive sexual pheromones from urine and glands, possibly vaginal and vulvar secretions and the scent marks in the environment.²⁴ Odor produced by intact tomcats and valeric acid, or a mixture of fatty acids, produced by the estrous queen act as sexual pheromones. Tomcat odor released during urine spraying for territorial marking is androgen-dependent and disappears after castration. Its source is uncertain, but may be part of a lipid component of the urine and/or it may be produced by the anal glands. During estrus, valeric acid is present in vaginal secretions. Tomcats may show an open-mouth flehmen response when sniffing urine, but anosmic sexually experienced males continue to mate. In tomcats, the odor of valeric acid induces a restless and lively searching reaction, but no sexual connotations, while sexually mature intact queens respond by exhibiting typical estrous behavior, thus it may induce or facilitate estrus in other queens.⁴

Catnip leaves contain nepetalactone which produced a characteristic behavior response simulating the antics of estrous queens. This is an olfactory response via the vomeronasal organ but is considered not a feline sex pheromone or pheromone-mimic but a hallucinogen which induces pleasurable behavior in cats, independent of sex or the presence of gonads. This response appears to be inherited as an autosomal dominant trait.⁴

Cats utilize 3 methods of territorial marking including scratching; leaving visual marks and odor marks from foot gland secretion; the cat's human family and familiar objects are marked by cheek or head rubbing with secretions from glands at the cheek corners and in the supraorbital region; and tomcat urine spraying to mark territorial boundaries.²⁴ The author has observed tomcats spraying parked car wheels, a trait frequently displayed by male dogs.

Sexual behavior of the queen is considered the most stimulatory to attracting tomcats. Proestrous signs are usually minimal, with increased affection or occasionally aggression and a desire to be petted. Frequent urination is usually seen.⁶⁰ In proestrus or early estrus, a slight amount of clear watery vaginal discharge may be present. In one study, 20% of cycling queens showed a

0.5 to 2 day proestrus in which many queens have behavioral characteristics of estrus, attract tomcats, roll in front of them, meow, but will not allow mounting or copulation.^{22,35}

Estrous behavior in the queen in the absence of a tomcat usually includes persistent vocalization, rolling, rubbing, extreme affection, and with variable incidence and intensity, treading the hind legs, lordosis, and tail deviation. A slight anterior and lateral set to the ears is common, and an intense facial expression simulates that seen with aggression or fright. A repeated monotone howling for as long as 3 minutes at a time is common and may accompany treading and rolling. The estrous cry is given by the queen to indicate that she is in estrus and in presence of the male, an "appeasement" cry to stimulate the tomcat to mount. Restlessness, general uneasiness, pacing back and forth, may accompany any of these behavioral patterns. A general loss of appetite of both the queen and tomcat is common during the breeding season. Some queens may not exhibit typical behavioral signs at every estrus except for increased affection, but will when properly handled or exposed to a tomcat. Treading, lordosis and the typical copulatory stance with lateral deviation of the tail can be induced by flank stimulation, stroking the back, alternate strokes over the thigh or stroking the perineum. Rubbing or scratching the back of the neck or shoulders induce treading, but usually not the precoital stance. The ear and facial expression may be induced by all of these manipulations. Handling and stroking an estrous queen may cause enough neural stimulation to induce ovulation.^{3,22,37,49,57,58}

Once the female shows good copulatory signs, the waiting and watchful male will approach usually from the side and grasp the skin of the neck in his teeth. This usually takes 5 to 50 seconds. He next will place his forelegs over her shoulders and mount, and for 0.3 to 8 minutes he will position himself by straddling her pelvic area and treading along her flanks with his legs and possibly stroke or strum the queen's thorax with his front feet. The queen at this time reflexly varies her perineal area by lordosis until her perineum and vulva are almost horizontal. Her tail will be deviated laterally. When positioning is right the tomcat will start pelvic thrusting with his exposed penis and on contact, intromission and ejaculation and the queen's coital "cry" or "scream" usually takes 1 to 17 seconds followed by the queen quickly rolling or twisting out of the male's grasp and aggressively attacking the male if he doesn't move away quickly; this takes 0 to 1 seconds for dismounting. Immediately the queen displays a postcoital "after action" consisting of disoriented rolling, stretching and genital

licking and twisting, taking 1 to 7 minutes and a variable period, 0 to 5 hours of refusing attempts by the tomcat to remount. Usually the tomcat stays at some distance watching and protecting his territory. Freeroaming, other tomcats may challenge him and indeed other males may mate with this queen and if they are successful, resulting in a litter from different tomcats or superfecundation.^{22,34,60} In one study, copulations numbered 20 to 36 during 36 hours of observation and were more frequent during the first 2 hours (3 to 6 copulations) than any subsequent 2-hour period.²² In one study, estrus averaged 7.1 ± 0.8 days, even though a significant level of plasma progestins were present.⁴⁴ The average range of estrus is considered to be 5 to 8 days with a range of 3 to 20 days. Ten days or longer periods is considered prolonged. Duration of estrus is not greatly influenced by mating and induced ovulation, although some feel estrus may be one or 2 days shorter in average duration in mated queens.²² Other researchers have reported the opposite effect, with mated queens in estrus for 8.3 to 8.6 days and non-mated queens in estrus for an average of 6.2 days.⁵³ Occasionally a timid queen, low on the social scale in a colony of females and checked with an experienced breeding male, will express poor estrous behavior, have good estradiol-17B serum levels indicating active mature follicles, but not allow interested males to mount and breed.⁵³

Relative size of the male and female may influence the success of mating. Females that are too large or too small may make it difficult for a successful rapid coital act resulting in a frustrated and unsuccessful breeding male. This is especially a problem with young males or timid males that are hand bred. The activity of the male attempting to breed a female may be enough to induce ovulation although the lack of intromission and ejaculation has failed to deposit semen for fertilization.¹⁸

The coital "scream" or "cry" was at some time thought to be pain caused by the penile spines, but this reaction can be elicited in queens in or out of estrus, intact or spayed, with any instrument that invades the vaginal and cervical area.^{18,34,48}

The cat is an induced or reflex-ovulator. Either natural mating, mechanical stimulation of the cervix/vaginal wall with probes, exogenous luteinizing hormone (LH) or gonadotrophic releasing-hormone (GnRH), or in a few queens, other stimulation, such as handling, or rubbing against objects during estrus, petting or stroking, may be enough neural response to cause GnRH and LH release which then appears as spontaneous ovulation.^{22,37,53}

Experiments on the effect of genital desensitization on mating behavior and ovulation in the queen revealed that sensations from the vagina cause the appropriate behav-

ioral responses of queens to intromission. Ovulation in queens can be triggered by impulses from the vagina, as well as the cervix, received during intromission.²³

Most queens in the absence of coitus will have non-ovulatory estrous cycles throughout the breeding season (Chart VIII). The cycle then consists of waves of follicles producing estrogen followed by atresia of these follicles and an interestrus period with no luteal or metestrus period. The mean and duration ranges of proestrus, estrus and the interestrus periods and cycle interval are quite variable. Proestrus can really only be characterized early by the presence of a male or possibly with vaginal cytology. A length of 0 to 3 days has been reported for proestrus. Estrus may last 3 to 20 days, but most will average 7 to 8 days. The interestrus period will last usually 3 to 14 days during the breeding season, but may be as long as 30 days. The mean interestrus time ranged from 9 to 13 days. Thus the length of nonbred queens' cycles can range from 7 to 40 days with most cycles being 12 to 22 days long with a mean of 16 to 20 days.^{18,22}

In non-fertile or induced ovulation by instruments or

exogenous LH or GnRH, pseudopregnancy occurs with corpora lutea persisting for 3 to 7 weeks, with a mean of about 40 days followed by 4 to 10 days of anestrus. Thus the duration of pseudopregnancy from mating to the next estrus is usually from 35 to 70 days, the average is around 45 days.²²

Pregnancy in the queen lasts 64 to 69 days with an average of 66 days. Some reports have an average of 63 days with a range of 58–65 days which is probably based on timing from the last of multiple breedings.^{22,53} Successful litters have recorded gestation periods of 59 to 71 days. (See pages 104–107) Variations may also be due to breed difference, colony differences, litter size and possibly time of year.^{18,22} Occasional queens will show estrus during pregnancy and estimates of 10% of pregnant queens, typically around 21 and 42 days of pregnancy, may show sexual behavior. Possible superfetation can occur at this time.^{34,48,60} Some queens will be in estrus within 7–10 days following parturition and may conceive if bred at this time while caring for the litter they just queened. Most will show lactational anes-

DOMESTIC CAT

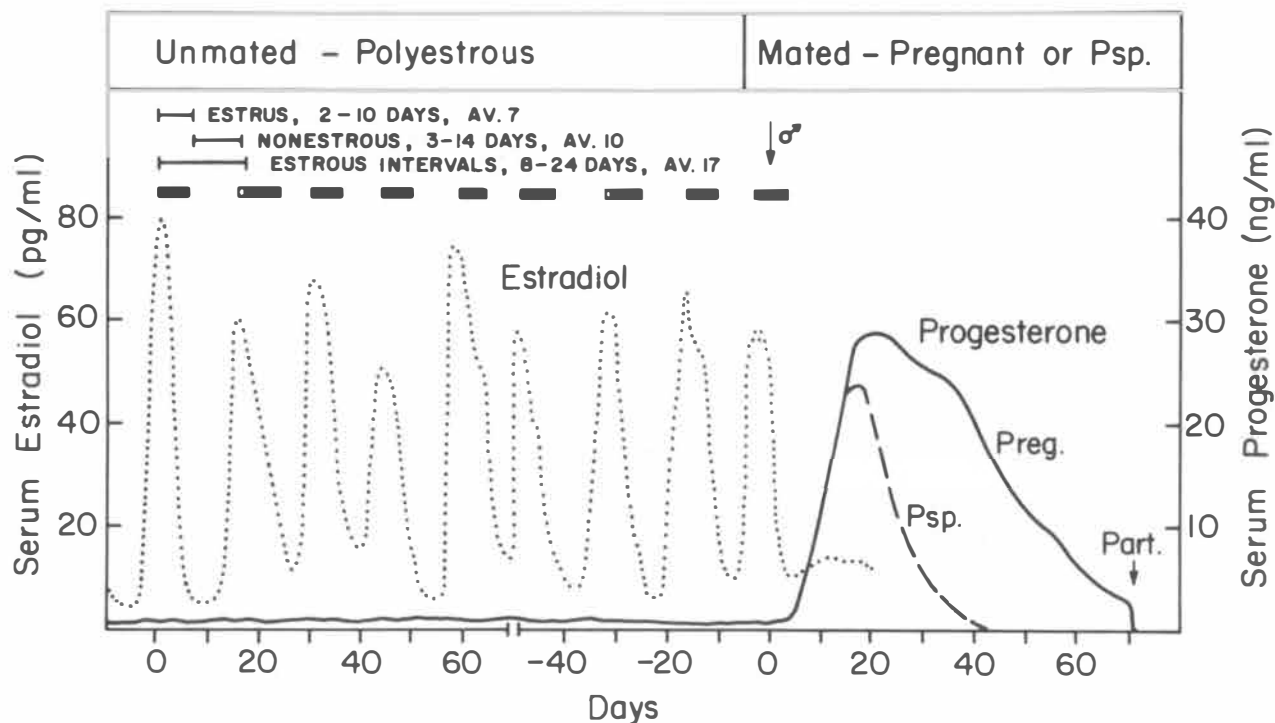


Chart VIII. A schematic representation of endocrine changes typically observed during polyestrous cyclic activity in unmated queens and during pregnancy or pseudopregnancy (Psp.) following fertile matings or vaginal stimulation resulting in ovulation. Solid bars indicate potential proestrus periods.

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trus and not return to estrus until 15 to 60 days (aver. 2–3 wks), while queens that have kittens that are removed from them within 3 days postpartum will return to estrus in 6 to 8 days. Post abortion estrus can occur within one week.²²

Sexual behavior and **vaginal cytology** of the queen are the two clinical signs best characterizing the estrous cycle. Several excellent articles on vaginal cytology in the queen have been reported.^{14,18,21,26,36,39,40,48,50,53} Vaginal cells are collected with a moistened sterile cotton swab (3 mm dia. Caliswab; Type 1, Inolex, subs. of American Can Company, Glenwood, Ill.), a 3 mm diameter smooth glass rod or by a clean glass eyedropper containing about 0.25 ml of sterile physiological saline solution. The collecting instrument is passed into the vagina about 1 to 1.5 cm by first inserting it into the vestibule in a dorsally directed manner and when resistance is met then redirect the instrument horizontally and place in the vagina. That way the clitoris and clitoral fossa are not entered or irritated. The moistened swab or glass rod are rotated and the fluid in the eyedropper is flushed 2 or 3 times in the vagina. The sample is placed on a clean glass slide and stained. Roll swab or glass rod on a glass slide for the best cytology or place fluid from eyedropper on a glass slide and either fix in alcohol immediately or air dry. Any good cytologic or hematologic stain can be used (See vaginal cytology for the bitch, p. 677). Keep the slides for reference of changes throughout the estrous cycle. Smears of vaginal cytology should be prepared every day or two when looking for changing ratios of cell types to determine the changes from proestrus to estrus to metestrus. The vaginal swabbing or flushing of some queens in estrus may induce ovulation.

No diapedesis of red blood cells is seen in the queen's vaginal cytology during any stage of the estrous cycle as seen in the bitch unless the vaginal cavity is traumatized when taking the sample, a genital tract infection is present, or slides are taken in the early postpartum period. Three basic epithelial cells are present. Parabasal cells are the smallest of the three. The cells are round to oval, and each contain a large clearly defined nucleus. Intermediate cells are larger than parabasal cells, the cytoplasmic borders are slightly angular and the nucleus is defined. Cornified cells show various signs of degeneration. The cytoplasmic borders are irregular or the cell is polyhedral. The cell may be folded or wrinkled; they look like "cornflakes." Vacuoles may be present in the cytoplasm. Nuclei may be pyknotic or absent or undergoing karyolysis.

In anestrus or prepuberty, scant parabasal cells, frequently in groups with tight intercellular bridges, are present. Debris may or may not be present and occasionally polymorphonuclear leukocytes will be present.

In proestrus, more mature cells will be seen as the vaginal epithelium responds to estradiol-17B with multiple layers of cells that become more mature at the surface. Few parabasal cells are seen, the number of intermediate cells are increasing and cornified cells are beginning to appear with more frequency as estrus approaches. Leukocytes are generally absent. At estrus the smear is dominated by cornified cells. Copious vaginal fluid and cells are present, but the fluid is watery and will wash instead of fix to the slide so that the background will be "clear" and lack the debris seen in the other stages of cycle. This is one of the earliest signs of the follicular stage of the cycle, or estrus.⁵⁰ In full estrus, 80% or more of the cells will be cornified.²⁶ Shille, et al. showed that the appearance of a relative increase in fully cornified (anuclear) polyhedral cells ("corn flakes") followed the rise in plasma estrogen levels in a majority of queens by 3 or 4 days and is in concert with the onset of estrous behavior.⁵⁰ These researchers also found that fully cornified cells (no nucleus) increased from 5% to 40% of the total cell population and intermediate cells (partially cornified with nucleus) decreased from 45% to 6% progressively for the 1 to 4 days of the follicular phase or estrus. Parabasal cells, generally low preceding estrus (1–6%) were absent on follicular phase days, 4 to 7 and the following days, cornified cells with pyknotic nuclei did not change much (40–50%) except for a slight increase during the follicular phase (50–60%). The author notices that the queen, unlike the bitch, may have good polyhedral large epithelial cells predominantly at estrus with most containing pyknotic nuclei, whereas in the bitch most of the cells will be anuclear at this stage.

If the queen does not ovulate, the cytology will regress back to proestrus and an anestrus type of cell appears. In early pregnancy or pseudopregnancy there are numerous cells and the reappearance of increasing numbers of intermediate and parabasal cells with a rapid decline in cornified cells. Leukocytes reappear, debris and mucus are present again. As pregnancy or pseudopregnancy progresses the smear will resemble that seen in anestrus with intermediate and parabasal cells predominant and less cells present although the background may contain a great deal of mucus. Queens that exhibit estrogen surges during pregnancy or at the end of gestation may reflect this in their vaginal cytology. If leukocytes are numerous in any smear and show indications of clumping in masses and advanced degeneration or toxicity, contain large numbers of bacteria and/or red blood cells are present, one should consider an inflammatory process and examine further.

The endocrinology and physiology of the estrous cycle, pseudopregnancy and pregnancy has been partially characterized and reported by a number of re-

searchers. 1,2,6,10,17,18,20,21,22,27,32,33,34,37,43,44,46,47,48,49,50,51,52,53,55,56,59,61,67

In proestrus, follicular growth and development associated with increased secretion of estradiol-17B occurs rapidly over a 2 to 3 day period just prior to the onset of estrus. The onset of estrus usually occurs as estradiol levels attain peak levels or during subsequent rapid decline. Levels from 5 to 20 pg/ml at basal serum measurement will peak to 40 to 100 pg/ml by or before the onset of estrus (Chart VIII). Levels usually greater than 20 pg/ml are closely associated with sexual attraction and receptivity.^{50,61} Levels decline during estrus as the fully mature follicles begin to undergo atresia. For the first 4 to 5 days of estrus, follicles retain the capacity to ovulate if sufficient copulatory stimulus is present, but how fertile these follicles are in protracted periods of estrus is unknown. Estradiol-17B levels rise and fall in sequential non-overlapping waves suggesting that follicles grow and degenerate as a group in nonbred queens although a few cats have shown overlapping follicular waves, more like that seen in the rabbit, another induced ovulator.^{50,53} Serum progesterone levels remain low (-0.5 ng/ml) throughout the non-breeding estrous cycle. Follicle stimulating hormone (FSH) is probably important in stimulating follicular waves, but no studies of levels in the cat have been reported.

Ovulation in the queen depends on the release of sufficient amounts of luteinizing hormone (LH) from the anterior pituitary, as in other species. Since the queen is a reflex-ovulator, LH is released on a neural reflex initiated by vaginal-cervical stimulation during coitus. Probably luteinizing hormone-releasing hormone (LH-RH) is first released from the hypothalamus following copulation which in time causes release of LH from the anterior pituitary gland. Exogenous LH-RH (25 ug) caused LH release from both anestrus and estrus cats and resulted in ovulation in the estrus cats.¹⁰ Luteinizing hormone (LH) in the cat fluctuates episodically with increases occurring every 20–30 minutes, probably under the influence of episodic release of LHRH. In castrated cats of either sex, the LH basal levels increased. Restoration of negative feedback was accomplished by administration of estradiol-17B, reducing LH concentrations to precastration levels.³² Concentrations of LH increased within 5 minutes after mating and usually reached a maximum within 20 minutes if a queen was limited to a single copulation.³³ This was similar to a single injection of LH-RH.¹⁰ A second mating one hour after the first resulted in a second similar increase in LH levels without evidence of a priming effect of the first mating on the LH release mechanism. Females allowed to mate at their own pace with several copulations during the first 2 hours showed LH release being evident during the first 90 minutes but copulations were ineffective in increasing the

peak levels of LH when mating continued beyond this point. There is no correlation between plasma levels of estradiol or progesterone. Repeated matings in the first 2 to 4 hours appear to be important in controlling the magnitude of the preovulatory LH surge.³³ In another study, less than 50% of fully estrous queens ovulated after a single copulation because of inadequate LH release, but most queens ovulated after 4 or more copulations.²⁰ Additional LH release became negligible after the first 1.5 to 4 hours.^{20,67} Following 30 copulations in 24 hours and 36 copulations in 36 hours, maximum LH release became negligible after the first 2 to 4 hours. The refractory LH release after 4 hours appears to be at the hypothalamic LH-RH release level, since exogenous LH-RH after these periods of multiple copulations and low LH levels after 2 to 4 hours will result in another immediate LH peak.^{21,22} Another study did show that LH release could be enhanced when coital inputs were repeated at 4 hour intervals indicating that the refractory period may be relatively short in cats.⁶¹ This occurred mainly in the 1st day and again at much lower levels of LH output on the second day (less than half the 1st day's peak) and no response on the third or fourth day.

Levels of plasma LH have been quite variable depending on the type of standard used in the test. Rat LH and cat LH standards have much higher levels than ovine LH standard (10% of cat or rat LH standards). Basal levels of 1.6 ± 0.4 ng/ml to high peak levels of 121 ± 24 ng/ml after multiple copulations are reported for the ovine LH standard compared to basal levels of 49 ± 19 ng/ml to high peak levels of 941 ± 154 ng/ml are reported for the cat LH standards.^{22,51}

Ovulation occurs within 25 to 30 hours after matings that cause release of sufficient LH; others reported up to 50 hours after mating. The differences in time and in some instances, no ovulations occur, may be the individual threshold levels of LH-RH and LH needed, days in estrus when mated, immaturity of follicles, and number of copulations required per individual for adequate release of LH; all may be quite different for individual cats. It appears that some cats will not release an ovulatory amount of LH until the second, third, or even fourth day of estrus.¹ Thus it appears that the best time to breed queens may be on the second or third day of estrus and to observe at least 4 or more coital acts to obtain adequate LH release and maximal ovulation.²²

Ovulation can also be induced in queens in estrus by stimulating the vaginal walls and/or cervix with a probe and just like multiple breedings, multiple repeated probings at 5 to 15 minute intervals will enhance adequate LH release.²² Ovulation can also be accomplished by injection of 25 to 50 I.U. of human chorionic gonadotrophin (HCG) with ovulation occurring in 26 to 27 hours.

Fertilization rates were nearly 100% for a natural service from the time of treatment through 27 hours, but declined to 35 to 80% from 30 hours to 49 hours after treatment. Conceptions occurred 52 or more hours after treatment, indicating the fertile life of the feline ovum after ovulation was about 24 hours.⁵⁴ Another study showed that a single injection of 500 IU of HCG produced a significant increase in mean percent ovulation rates in comparison to single injections of 0, 50 and 100 IU of HCG. Also administration of either 250 or 500 IU of HCG daily for 2 days of estrus resulted in a greater percent of ovulation than the 2 day injection of 50 I.U.⁶⁵ Administration of 25 ug of LHRH also caused ovulation in estrous queens.¹¹

Wildt, et al. by laparoscopic study have described the formation of the mature follicles, ovulation and corpora lutea.^{62,66} The ovary at proestrus will contain clear grayish areas with distinct borders that are 0.5 to 1.5 mm in diameter and at estrus become distinct fluid filled pre-ovulatory follicles. Mature follicles measure 2.5 to 3.5 mm in diameter and develop to this state in 24 to 48 hours. Non-ovulated follicles will regress to a nondetectable state in 3 to 7 days. As ovulation approaches the follicle dome becomes clear in appearance while the base at the surface of the ovary becomes heavily vascular. Ovulation is gradual, culminating in the release of a yellowish-gray mound-like mass that often adheres to the surface of the ovary. Hemorrhage at the site takes place and a cratering of the follicle's dome appears. Within 24 to 36 hours postovulation, luteinization and maturation of the corpus luteum takes place. It changes from a dark red to an orange-yellow color. The mature corpora lutea are raised above the surface of the ovary and contain a flattened dome. Corpora lutea reach a maximum diameter of 4.5 mm. Regressing corpora lutea are small yellowish flat luteal scars that may remain visible on the ovarian surface for up to 6 weeks.

Sterile matings, exogenous LH or LH-RH, and occasional "spontaneous" ovulation result in **pseudopregnancy**. Corpora lutea are formed within 1 to 3 days and persist for 3 to 7 weeks postovulation. Progesterone levels rise over 1 ng/ml by day 3 after ovulation and reach peak levels of 15 to 90 ng/ml by day 15 to 25 and thereafter decline (Chart VIII). Progesterone levels return to 1 ng/ml within 30 to 50 days, although reports of duration of pseudopregnancy as the interval from mating to the next estrus range from 35 to 70 days with the average being 45 days.^{22,44,52,61} Following a fertile mating and ovulation 25 to 30 hours after sufficient release of LH, oocytes are fertilized by the ejaculated sperm that requires about 1 to 2 hours for capacitation in the female reproductive tract. Sperm recovered from the ductus def-

erens of male cats were capable of fertilizing recently ovulated feline ova in vitro without in vivo capacitation. This may indicate that epididymal or ductus deferens sperm are different from ejaculated sperm or indeed capacitation is not required.⁵ Oocytes remain fertile for up to 48 hours. **Oviduct transport of fertilized oocytes** takes 4 to 5 days. Migration of blastocysts in the uterine horn takes place for 6 to 8 days and implantation occurs around day 12 to 14.^{18,22,55}

Endocrinology of pregnancy—The progesterone plasma levels in early pregnancy are similar to those seen in pseudopregnancy until implantation takes place at about day 12 to 14 (Chart VIII).⁵⁹ Progesterone plasma levels were 13 ng/ml on day 50 versus 2 ng/ml and 4–5 ng/ml on day 62 versus 1 ng/ml in pregnant and pseudopregnant queens, respectively. Elevated progesterone blood levels in pseudopregnancy coincides with implantation in the pregnant cat and again on about day 28 when the first appearance of regressive luteal changes in the pseudopregnant cat are seen.⁵³ At this time, blood progesterone levels increase in the pregnant queen, while levels in the pseudopregnant queen decline. At 28 days the progesterone levels in the pregnant queen are also enhanced by an increase in placental progesterone.^{18,38} Corpora lutea of pregnant queens persist and produce progesterone until 40 to 50 days when placental production of progesterone is adequate to maintain pregnancy.³⁸ Ovariectomy performed between 45 and 49 days or later will not effect pregnancy and normal kittens will be born at term.^{22,48,53}

Parturition is accompanied by a decline in progesterone to basal levels, but detailed studies are needed to determine if the serum progesterone levels fall to basal levels preceding or following placental expulsion.²² Estradiol-17B is elevated above the base level of 9 pg/ml between Days 58 and 62 and declines sharply just before parturition.⁵⁹ Pregnant queens treated with FSH on Days 33–37 and HCG on Days 38 and 39 developed follicles (av. 9.3 follicles/cat), ovulated (av 3.4 corpora lutea/cat), and exhibited behavioral estrus (5/7 cats). Estradiol-17B levels gradually increased but serum progesterone levels remained constant in the treated cats while in control cats levels gradually declined as expected. Gestation periods and litter size were not significantly different between treated and control queens.¹²

Prolactin (PRL) levels were measured using canine PRL antisera by Banks, et al.² PRL blood levels were elevated the last third of pregnancy (31.2 ± 5.1 ng/ml.). The last 3 days of gestation, levels increased to 43.5 ± 4.5 ng/ml. Suckling stimulus maintained PRL levels at 40.6 ± 7.2 ng/ml for the first 4 weeks postpartum, and 27.8 ± 3.1 ng/ml during the last 2 weeks of lactation.

Following weaning, levels decreased to approximately 15 ng/ml with basal levels of 7.3 ± 0.6 ng/ml maintained after the second week. Pseudopregnancy had no effect on PRL levels in the queen.

Induced abortion—Feline corpora lutea are very resistant to the luteolytic effect of prostaglandins and bromoergocryptine, both of which cause luteolysis in the dog after 30 days of pregnancy or pseudopregnancy.²² Queens one and two weeks pseudopregnant were treated with 0.5 to 5.0 ug/kg of PGF₂ with no significant effect on progesterone levels.⁶⁴ Repeated administration of PGF₂ every 12 hours with either 220 or 440 ug/kg on days 11 to 15 or 21 to 23 postcoitus did not cause a significant drop in progesterone during the second week. During the fourth week, significant reduction took place, but did not cause complete luteolysis and did not reduce the length of pseudopregnancy.⁵² PGF_{2a} (500 to 1000 ug) given twice subcutaneously, 24 hours apart, caused abortion in queens after day 40, but not before. Abortion occurred within 24 hours after the initial injections in 9 cats and after the second injection in 4 cats.⁴¹ Pregnancy was also terminated in cats by administration of a combination of ACTH and PGF_{2a}.⁶⁸

Pregnancy diagnosis is best accomplished by careful palpation of the uterus per abdomen from days 17 to 25 when the conceptuses are in a round segmented condition. After days 30–35 the elongated fetus and fetal membranes become confluent and it is difficult to ascertain pregnancies from an enlarged uterus.^{18,22} Radiographs will show the mineralized opaque fetal skeleton from 40–45 days of gestation to term. Approximate gestation age can be made by radiographic appearance of mineralized bone in the fetus, ie. 41 days, the radius and ulna, 43 days, tibia, fibula, ilium and ischium and occipital bones of the skull, at 55 days, the axial skeleton can be visualized.¹⁸ Breeders often depend on the physical change of nipples from light pink to rosy pink in the second and third weeks following copulation as indicative of pregnancy.²⁷ (See pages 14–33)

The endocrinology and physiology of parturition in the queen has not been fully studied. Certainly there is a decrease in progesterone to basal levels and an increase in estradiol 17-B a few days just prior to queening and a drop the day of queening and an increase in PRL levels. The endogenous effects and levels of prostaglandins, relaxin, cortisol and oxytocin are not known. Clinically, oxytocin is very effective in causing uterine contractions for uterine inertia, retained kittens or placentas and milk let-down. Probably endogenous oxytocin is present. The queen will react to "feathering" the vagina during parturition resulting in uterine contractions. Rectal temperature does fall in the first stage of

labor, similar to the bitch.⁴⁸ The queen will search for a warm, dark, secluded place and nest. The last 2 weeks, gland development and the last day, milk secretion are present. The second stage of labor is usually quite rapid with a few abdominal strains, similar to defecation, and a kitten will be delivered. One or two may be born, are cleaned vigorously by the queen and the cord severed by biting. Placental expulsion, the third stage of labor, follows the fetal delivery quite closely and the placenta is consumed by the queen. Usually the next kitten is presented in less than an hour. If the queen is disturbed, especially if not confined or even if confined, labor may cease, kittens may be moved, nursed and then continuation of queening, hours or days later. The longer intervals between births may be superfetation.

To sex kittens on the day of birth the anogenital distance is measured with a soft, pliable plastic millimeter ruler. Males ranged from 11 to 16 mm and females, 6 to 9 mm at birth, 14 to 21 and 8 to 13 at 21 days of age, 16 to 23 and 10 to 15 at 42 days of age, respectively.⁷

Induction of estrus in queens can be accomplished in several ways; lengthening of the light cycle 14 to 18 hours per day, socializing of queen with other cycling queens and/or exposure to a tomcat, use of sex steroid hormones and gonadotrophins. Induction of queens with gonadotrophins may lead to large numbers of follicles which may not contain mature ova, or may lead to cystic follicular degeneration. Excessively long periods of estrus may be encountered with the use of either gonadotrophins or sex steroid hormones.¹⁹ Induction of estrus has been followed by successful matings when using a daily intramuscular injection scheme of pregnant mares serum gonadotrophin (PMSG) for eight days, the dosage depending on time of the year (Chart IX) as reported by Colby.^{16,19} The dosage may be reduced to 25 IU. as estrus behavior becomes apparent to prevent overdose problems. Estrous behavior should be judged daily by a handler or by placing the queen with an experienced tomcat. This regimen should not be used in queens under 1 year of age because of production of cystic ovarian follicles. The best age group is probably from 1 to 5 years. Litter size decreases with older queens. The results are reported by Colby to be 80% efficient. The guidelines given above are important to follow with any of the hormone regimens used for induction of estrus.

Another method has been described using a single injection of 100 IU of PMSG followed in 7 days by 50 IU of HCG which produced results comparable to natural breeding.¹⁵ Follicle stimulating hormone-pituitary (FSH-P) has also been used to induce estrus. Administration of 2 mg of FSH-P intramuscularly daily for 5 days unless

Calendar Months	Day							
	1	2	3	4	5	6	7	8
	PMSG (IU)							
December–January	100	50	50	50	50	50	50	50
February–August	100	50	50	50	50	25*	25*	25*
September–November	100	50	50	50	50	50	50	50

*In cats near estrus (behavior), dose decreased until bred.

Chart IX. Induction of Estrus in Cats by PMSG

(E. D. Colby,^{16,19} and courtesy and with permission of P. W. Concannon and D. H. Lein and publisher, W. D. Saunders Co.²²)

the queen shows estrus before 5 days; results in most showing estrus in 4 or 5 days. On day 1 and 2 of estrus, 250 IU of HCG are given intramuscular to enhance ovulation. Queens should be bred at least 4 times on each day of estrus for a period of up to 4 days. Mean litter size was normal.^{45,63} This regimen was used successfully to produce litters by using frozen cat semen.

Estrogens (50 mcg of estradiol benzoate or 0.25 mg of estradiol cypionate (ECP), given IM and repeated in 48 hours) will induce estrus in most queens.^{18,22} No more than 8 mg of estrogen should be administered within any continuous 4 month period to avoid toxicity or extreme bone marrow suppression.⁵⁶ Testosterone can also be used at 20 mg/day, intramuscular, to induce estrus in the queen.¹⁸ Either excessive use of estrogens or testosterone in the queen may initiate estrus that will last for 2 to 4 weeks unless natural or artificial coitus is provided.

Estrus control in the queen using progestins has been successful in Europe and Australia; medroxy-progesterone acetate ("Perlutex," Leo Laboratories, Ltd., Middlesex, England and "Anobulin," Berk Pharmaceutical Ltd., Surrey, England) has been used successfully in both oral and injectable forms. These are not approved or available in the United States. Megestrol acetate ("Ovaban," Schering Corp., Kenilworth, N.J.), is marketed for dogs to control estrus, but has been experimentally and clinically used to control estrus in cats. Progestins when administered are believed to mimic the corpora lutea and have a negative feedback on gonadotrophic-releasing hormones. Megestrol acetate, 5 mg daily for three days will control signs of estrus within 5 days. Queens were then given 2.5 to 5 mg once weekly which kept them in anestrus for up to 2 years with successful estrus and pregnancies following. This regimen should be used only in young queens that have experienced estrus. It can also be used in nonestrous queens to maintain an anestrus state.^{22,28} This drug has also been used to control urine spraying in tomcats and queens (5 mg/day until spraying is controlled, then 5 mg/week) and in the treatment of miliary dermatitis and control of eosinophilic

granuloma. Progestin therapy may cause increased appetite, increased body weight, a calming effect, and increased affection. Prolonged and indiscriminate use may produce a Cushingoid syndrome.^{13,22} Cats with genital tract infections should not be administered progesterone or progestins. Indiscriminate use of progestins can lead also to cystic endometrial hyperplasia-pyometra complex, hypertrophy and hyperplasia of mammary glands and possible mammary gland neoplasia.²² It appears that progestin compounds result in much less uterine disease in the cat compared to the dog. In a small field trial it was reported that either 5 mg of megestrol acetate (MA) or chlormadinone acetate (CAP) given orally once at early estrus completely prevented gestation and that this was accomplished for 15 estrous periods. This queen did have successful pregnancies during and after the use of these progestins. Two tomcats received either 5 mg of MA or CAP or 2.5 to 5 mg of delmadinone acetate (DMA) orally on a weekly basis to control sexual behavior with no side effects and the return to sexual activity within 8 to 10 days after discontinuing the progestins.³¹

"Mibolerone," a synthetic anabolic steroid ("Cheque," Upjohn Co., Kalamazoo, MI) is an approved contraceptive used to control estrus in young bitches. Estrus was prevented in queens when administered at a daily dose of 50 ug for a 180 day period. There was no apparent effects on subsequent estrus, mating, queening, litter size, or developmental defects in neonates. The mechanism of actions of this androgen, like progestin, is to suppress release of pituitary LH. Side effects consisted of increased thyroid weight, decreased thyroid function, increased serum cholesterol levels, slight masculinization of neck skin and clitoral hypertrophy in some cats. Formation of a cartilaginous or osseous penile baculum and central retinal degeneration and chorioretinitis were seen in a few cats.⁹

An extensive review by Colby described other non-approved drugs that may or may not be available in the United States for estrus suppression in the queen such as "Provera" (medroxyprogesterone acetate), "Orgaster-

one" (methylloestrene), and DMA (delmadinone acetate).¹⁹ Burke cited the use by Europeans of 1% pilocarpine solution for 2 to 4 days to stop estrus in queens within 2 days. No mechanism was given.⁸

Mismatched queens can be successfully treated with as little as 0.125 to 0.25 mg of estradiol cypionate (ECP) given 40 hours after coitus or within the first 5 days post coitus. The ova are retarded in transport through the oviduct for at least 6 days instead of 4 to 5 days, resulting in degeneration in the late proliferative state instead of the secretory phase.^{22,25}

Repositol diethylstilbesterol, a product not available in the United States has been used for mismatching at the level of 2 mg on day 2 and repeated on day 10 following coitus. All estrogen therapies will extend the period of estrus and will cause accumulative effects to cause toxicity and myelosuppression if overdosed.^{19,25}

Abortion may be induced in cats over 40 days of gestation or live newborn after 55 days with PGF_{2a} at doses of 0.5 to 1.0 mg/kg of body weight given twice at 24 hour intervals.⁴¹

The control of free-ranging cats in the United States has become an important issue in the last 20 years. Few accurate studies or estimates of this population and means of control have been studied. One study in Manhattan, Kansas estimated that the population in that city increased by 18% annually and that 59% of the females were spayed. It was calculated that 88% should be spayed to maintain a zero population growth.⁴²

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Reproductive Physiology of the Queen

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Anatomic and Congenital Defects, Intersexes

Anatomic or congenital defects or abnormalities of the reproductive system in bitches and queens are rare but have been reported.^{23,109,239} Hare in his report considered intersexuality rare in the dog. His review reported on 48 spontaneous and 52 drug-induced cases.¹⁰⁹ Of the 48 spontaneous cases, 16 were Cocker Spaniels and 5 Beagles.^{73,109,110,162,179}

The differentiation of sex occurs prenatally and is expressed finally by events that occur at puberty. In normal development, an XY genotype will cause induction of primary medullary sex cords and a normal functioning testis will form. In the XX genotype, or more likely, the absence of a Y chromosome, the medullary sex cords regress and the secondary or cortical sex cords are induced and an ovary develops. A number of abnormalities have been observed to occur with both normal XX and XY genotypes and especially with abnormal genotypes (XO, XX/XY, XO/XY, XX/XXY or XXY).

The development of either a Wolffian (male) or a mesonephric duct system or Mullerian (female) or paramesonephric duct system, although both are present in the prenatal state, takes place resulting in either epididymis and vas deferens in the male, or oviducts, uterus and the cranial one-third of the vagina in the female. This development depends on the secretion of hormones by the fetal testis, an inhibitory hormone now called Mullerian inhibiting factor (MIF), a nonsteroid macromolecular factor is produced by the fetal Sertoli cells. MIF inhibits development of the paramesonephric duct and an androgen-like hormone from the fetal testis stimulates the development of the mesonephric system. The ovary has little influence, but the total aplasia of gonadal tissue results in a rudimentary paramesonephric (female) duct system.²⁵¹

The phenotypic sex involves the organogenesis of the urogenital sinus and external genitalia, probably the descent of the testis is under the influence of an androgenic-like hormone from the fetal testis which results in male external genitalia, whereas, the lack of this androgenic-like hormone results in a female external genitalium. Excess circulating androgens, exogenous or adrenal gland source, will cause masculinization of the urogenital sinus but has little influence on prior developed mesonephric or paramesonephric duct systems.

Hermaphroditism or intersexuality occurs because of faulty differentiation and/or function of the fetal gonads and results in a deficiency of male-stimulating or female-inhibiting hormones, or there is a loss or reduction of sensitivity to a hormone on the part of a receptor organ. Induction can also take place if an excess of androgen-

like hormone is produced either endogenous (congenital adrenogenital syndrome) or given exogenously.¹⁰⁹

Hermaphrodites are classified as true hermaphrodites if both male and female gonads are present in any of 3 forms; bilateral, ovotestes present on both sides, unilateral, ovotestes on one side, and either testes or ovary on the other and bilateral, with ovary on one side and testes on the other. A male pseudohermaphrodite has testicular gonadal tissue and genital organs with some female characteristics. A female pseudohermaphrodite has ovarian gonadal tissue and genital organs with some male characteristics.

In Hare's review of 48 cases, 25 of the 48 were male pseudohermaphrodites, with 13 having an enlarged clitoris, 10 an underdeveloped penis and the testes usually were abdominal, but occasionally one was found in the inguinal canal or scrotum. All but 2 of 25 had some development of Mullerian duct systems. Thirteen of 48 were true hermaphrodites. All had clitoral enlargement with or without an os or underdeveloped penis, with Mullerian duct development. Seven cases had some Wolffian duct development. Two of 48 cases were female pseudohermaphrodites with masculinization of the external genitalia and development of a penis and prepuce. The genetic sex determination showed that 7 of 25 male pseudohermaphrodites were XY and 5 were XX. While 5 of the true hermaphrodites were studied and 3 were XX, one a possible XX/XXY and another a possible XX/XY. All female pseudohermaphrodites studied were XX including the 52 drug-induced cases.¹⁰⁹

Exposure of female fetuses to exogenous androgens between the 4th and 7th week of gestation results in masculinization of the genital ducts and urogenital sinuses. Early exposure may lead to almost complete formation of an epididymis, vas deferens, male urethra, prostate and penis. Exposure after 50 days of gestation results in clitoral enlargement only. These latter animals have normal ovaries, Fallopian tubes, a uterus and may be fertile.²⁵¹ Forty-five female pseudohermaphrodite pups of 87 offspring were produced by feeding 14 bitches methyl testosterone throughout pregnancy.²³¹

Exposure of female fetuses to exogenous estrogens during the sensitive period of sexual differentiation can lead to incomplete fusion of the caudal Mullerian ducts, incomplete fusion of the urogenital sinus, incomplete formation of the vagina and induction of prostate development. Exposure after sexual differentiation results only in hypertrophy of the uterus.²⁵¹

Female fetuses subjected to exogenous progesterone may result in limited masculinization. Various synthetic progestogens are quite androgenic and can produce virilization of female fetuses. The first sign of

virilization in newborn pups is the displacement of the orifice of the urogenital sinus, resulting in the vulva assuming a ventrocranial direction. This usually occurs when the fetus is exposed between the 30 and 50 days of gestation. Clitoral enlargement may also be seen.^{72,251}

Exposure of male fetuses to excessive exogenous estrogens in-utero may lead to feminization of the genital tract resulting in partial regression of the Mullerian ducts and insufficient gubernaculum outgrowth and hypospadias. Hypospadias may also be seen with excessive progesterone, especially synthetic progesterone and also with antiandrogens (megestrol acetate, chlormadinone acetate and cyproterone acetate). The antiandrogens may also cause complete inhibition of the Wolffian ducts and a female type of development of the urogenital sinus. No genital duct systems may be found since Mullerian duct regression is normal.²⁵¹

A history of difficulty in determining sex, urinary incontinence, abnormal or bloody discharges from the urogenital opening, abnormal external genitalia and position, a complaint of the males or females assuming the stance of the opposite sex when voiding are all common in intersexes. Intersexes should be examined systematically. A detailed history of therapies during pregnancy, examination and/or history of siblings with similar problems and a complete physical examination usually reveals a female with an enlarged clitoris or a male with an underdeveloped prepuce and penis or a degree of hypospadias and a lack of scrotal development.

A definitive diagnosis of pseudohermaphroditism or true hermaphroditism requires exploratory surgery or removal of the gonads and genital tract for histological section, sex determination by karyotyping and sex chromatin determination.⁷³ Removal of an enlarged clitoris may be esthetically desirable and corrective surgery if possible of urethrovaginal fistulae may be necessary. Retrograde contrast urethrography or pneumocystography may be needed to define urethrogenital tract abnormalities.¹³⁴

Neoplasia of retained testis, especially with the formation of Sertoli cell tumors in male pseudohermaphrodites, development of feminizing syndromes, attraction of males and cystic endometrial hyperplasia-endometritis-pyometra in remaining Mullerian systems requires surgery for correction of these problems.^{40,155,191}

Ovarian agenesis, hypoplasia and aplasia of portions of the Mullerian duct system in the bitch have been described.¹⁷⁵ Uterus unicornis is occasionally seen in the bitch and has been reported. Partial fusion and unequal length of uterine horns may occur in the bitch.¹⁷⁵ Remnants of mesonephric or paramesonephric ducts may be found parovarian, parametrial or in the fimbriated end

of the oviduct where they are called hydatids of Morgagni. Cysts of Gartner's ducts in the bitch are rare.^{25,26} A persistent postcervical band caused a dystocia in one bitch.¹²⁰

Hypoplasia of the vulva, persistent hymen, vaginal/vestibular strictures, congenital vestibulovaginal stenoses, segmental vaginal aplasia, vulvovaginal clefts, double vaginas have all been reported in the bitch.^{22,127,143,200} Vestibulovaginal stenosis was reported in 22 maiden bitches of various breeds with clinical signs of vulvar pruritus, incontinence, and vaginal inflammation, perivulvar dermatitis, and/or difficult mating. Thirteen of these bitches had vestibulovaginal strictures and 9 had a persistent perforated hymen.¹²⁷ Diagnosis is frequently made by digital palpation. Vaginoscopic examination or radiography with contrast media or pneumocystography may be needed to diagnose cranial vaginal tract strictures or stenoses. Digital dilatation, vestibulo-vaginoplasty, vaginectomy or vaginotomy may be needed to correct these conditions.

The author has seen cases of vestibulovaginal strictures or dorsal perivaginal folds with an inverted deep-set vulva in many bitches. Most are found at mating with bitches refusing copulation or males not successfully penetrating and "tying." Others have been found on routine prebreeding examination which should always include a digital exam of the vestibular-vaginal area when a hypoplastic vulva or a single or multiple fibrous strictures are found in the vestibulovaginal area.

In the author's experience, this condition is best treated with digital expansion or dilatation, or if this is not possible, artificial breeding. At parturition only an occasional bitch will require an episiotomy or caesarian section. Most will dilate with the hormones of parturition and be normal postpartum.

The author has seen this condition most frequently in German Shepherd bitches. Wadsworth and coworkers described a mid-vaginal imperforation in 3 Beagle bitches with mucoid material distending the vagina cranially and multiple fluid-filled submucosal cysts of possible Gartner's duct origin in one bitch.²⁴⁸ The author has also seen 2 similar cases. Hematocolpos or hematometra may occur secondary to congenital atresia of the Mullerian duct system.

In the queen, rare cases of intersexuality are reported.²³⁹ Cystic rete tubules in queens of any age are quite common.^{175,239} Uterus unicornis has been reported with a 1 in 1000 incidence and this may be associated with renal agenesis on the same side.^{216,232} Gartner's duct cysts, Bartholin's gland cysts, paraovarian and parametrial cysts, and cysts of the fimbriated end of the oviduct in the cat are rare.^{25,26} Segmental aplasia of the uterus

has been seen in the queen by the author. Cystic rete ovarii tubules in queens of any age may be seen.^{175,239}

Tortoise-shell or black and orange cats are invariably female and when male are usually sterile since the orange coat color and its alternate black, are determined by genes within the X chromosome and are sex-linked.^{150,167,239}

Nutritional Aspects

Nutritional causes of infertility in the bitch were reported by Mosier.¹⁸⁵ Several commercial dog food companies have completed research on the requirements for breeding, pregnancy and lactation in bitches and the results of deficiencies in proteins, calories, fats, minerals and vitamins. A 5 to 10% increase in the total maintenance diet will result in "flushing" a bitch during proestrus leading to a larger-sized litter. Researchers reported that protein deficiency in the dog leads to a reduction in blood levels of gonadotropic hormones.¹⁶¹ The additional 5–10% increase in dietary intake must be discontinued during estrus and the first 2 or 3 weeks of gestation or the rate of embryonal death will increase.

Vitamin K deficiency in puppies is characterized by hemorrhage around the mouth and nose and is seen when dog food is improperly stored for long time periods. Puppies with poor muscle strength, myodegeneration and/or anemia may need Vitamin E supplementation, while puppies that are not content, cry frequently but come from healthy bitches may have Vitamin B-complex deficiencies and may have come from bitches fed a low thiamine diet. Liver in the diet of pregnant bitches, 2 or 3 times weekly, is an excellent source of B-complex vitamins, vitamin K, phosphorous, high quality protein and causes increased lactation and increased placental size resulting in increased fetal nourishment.

Excess supplementation of calcium can cause zinc deficiency, resulting in uterine inertia and subinvolution. A ratio of calcium to phosphorus should be maintained at 2:1. Zinc can be increased by giving zinc sulfate or gluconate tablets or feeding liver. Excess Vitamin D leads to tissue calcinosis, premature closure of the cranial vault, calcium deposits on the tongue and liver surface, and kidney disease and death of pups before 1 year of age. National Research Council, (NRC) recommends a Vitamin D intake of 8 to 9 units per pound daily.

The NRC nutritional requirement for a pregnant bitch recommends a protein requirement of 25% of food on a dry weight basis, but some commercial dog foods contain 20 to 22% protein and usually contain higher cereal content which causes lysine deficiency resulting in increased puppy mortality at birth and an abnormal liver-

brain ratio (normal 2 to 1). A 25 to 30% protein level should be recommended for pregnant dogs, toy breeds should be about 30% and animal protein is favored over plant protein for puppy survival rate. Again, liver is an excellent source of protein and 1/2 to 1-1/2 ounces can be given 2 or 3 times a week. Cottage cheese and fish meal are two other good protein sources. Fat content should range from 7 to 9%. Insufficient fat results in linoleic acid deficiency, which can be supplied by adding corn oil or vegetable oils, but greater than 5% of caloric intake causes excess linoleic acid resulting in hemorrhage, anemia and muscle degeneration in puppies. Even though caloric requirements are increased by adding fat, no more than 4% above the 7–9% recommended should be added since puppy weight decreases and puppy mortality may increase by up to 30%. Carbohydrate should not be more than 57% of a pregnant dog's diet. During lactation, diets containing 28 to 30% protein, and 20 to 25% fat are very effective in stimulating lactation and puppy growth.

The puppies condition at birth will reflect the nutrition of the bitch. Three factors are measured: weight at birth for the breed, liver-brain ratio and fat at the kidney hilus. Puppies that are underweight for the breed at birth are usually undernourished. The bitch may have been under-nourished or inadequately fed too much fat, carbohydrate, or inadequate quantity or quality of protein. The liver-brain ratio by weight should be 2 to 1 with the liver being at least 1-1/2 times heavier than the brain. Fat should be present in the kidney hilus of the puppy if the bitch received adequate caloric intake. If the bitch has poor labor at whelping, an imbalance of calcium-phosphorus-zinc ratio may be present. During pregnancy a bitch should show a 5–10% weight gain. If a bitch loses weight during the gestation period, puppies will be poor growers and have an increased mortality rate. If a bitch receives marginal feed early in pregnancy, then supplemented later, the puppies will usually show increased obesity.¹⁸⁵ As in other animals, bitches with severe emaciation will have delayed puberty and anestrus. Obese infertile animals should be checked for hypothyroidism.

In a study of preferences for diets containing sucrose over a bland diet, both female and male dogs preferred the sucrose diets over bland diets, but bitches had a greater preference for the 1% sucrose diet than males with no difference noted at concentrations of up to 20%. Daily caloric intake was lowest in bitches during estrus, higher during metestrus and highest at anestrus. Ovariectomized bitches had higher food intake and weight gain than sham-operated bitches for the first 10 days post-operatively.¹³⁰

Another study showed that Beagle bitches fed two different diets from 3 weeks post conception, one containing 44% metabolizable energy from carbohydrate and another containing 0%, had similar numbers of pups at whelping, but fewer pups from the carbohydrate free diet were alive at birth (63% vs 96%) and only 35% of the pups were alive at 3 days of age. Plasma glucose levels, as well as alanine and lactate were depressed, while free fatty acids and B-hydroxybutyrate were elevated in bitches in late gestation on the carbohydrate-free diet. Milk from these bitches was low in lactose and high in fat.²¹⁷

Hormonal Disturbances—Anestrus, Ovarian Cysts, Hypothyroidism and Others

Hormonal disturbances, imbalances or abnormal expression of estrus, either exaggerated, prolonged, split, short, shallow or silent, **or anestrus in the bitch and queen** have been noted by clinicians and observed by the author. These cases have not been well-documented by clinical and/or research studies since repeated examination, hormonal assays of gonadotrophins and sex steroid hormone levels, daily recording of sex behavioral and vaginal smear changes are time consuming, expensive and may not be practical for the average pet or kennel owner. Most of these studies have been carried out by reproductive physiologists studying normal bitches and queens throughout their reproductive cycles. The association of infertility and hypothyroidism in both the female and male dog has been well-documented and this can be diagnosed and documented with a single blood test and treated with thyroid supplementation.^{212,219}

It is well-known that reproductive changes are seen with increased age in dogs of both sexes. In the male, increased testosterone levels or constant testosterone secretion over the years will lead to cystic prostatitis, perianal or circumanal gland adenomas. Castration will alleviate these conditions if neoplasia has not occurred. Examination of the testes may reveal single or multiple functional Leydig cell tumors and increased testosterone levels. Temporary relief can be achieved with exogenous estrogen therapy. The aging intact tom cat appears to have less reproductive tract pathology than the stud dog.

In the bitch and queen, either prolonged repetitive secretion of estrogens followed by progesterone from multiple non-pregnant cycles, cystic follicular degeneration, luteal cysts, or granulosa cell tumors, can all cause cystic endometrial hyperplasia, hydrometra, pyometra, mammary gland hyperplasia and tumors, inguinal hernias and possible alopecia of the ventral portion of the body. **Cystic endometrial hyperplasia and its associ-**

ated complications of endometritis and pyometritis can be seen in bitches following several non-pregnant cycles at 3 years of age with an increased incidence with advanced age. Dow has shown that either prolonged estrogen and/or progesterone administration in the bitch and queen will cause cystic endometrial hyperplasia and pyometritis.^{81,82,83,84,87} (See later section) Therefore, it is a good practice to breed bitches and queens at an early age or probably use steroid contraceptives to delay pregnancy but maintain a normal uterus. Once litters are produced, and others are desired, several non-pregnant cycles should not be permitted since the same syndrome may develop. As soon as a bitch or queen are finished with producing litters, an ovariohysterectomy should be performed to alleviate the potential threat of pyometritis and ovarian cysts or tumors.

Ovarian cysts, commonly observed in dogs and cats, increase in incidence with age. One study reported nearly 90% of older female dogs having ovarian cysts.^{24,25} Frequently these are not functional follicular cysts but are expressions of hyperplasia of remnants of rete ovarii, mesonephric or Wolffian duct (parovarian cysts), paramesonephric or Mullerian duct or invasion or downgrowth of surface epithelium called epithelial tubules, causing sub-epithelial structures (SES) or sex, egg or granulosa cell cord hyperplasia. All of these cysts in the bitch increase with age and are probably due to sex steroid stimulation. Only 3% of older Beagle bitches had functional follicular cysts in one study.⁶ Functional cysts, such as follicular cystic degeneration and luteal cysts reported in cattle are seen in the older intact bitch and queen and may lead to hyperestrogenism or prolonged low levels of blood progesterone. Sex steroid levels, sexual behavior, vaginal cytology, vaginoscopic and laparoscopic examinations are all useful in the clinical diagnosis of these conditions.

Anestrus in the puberal bitch may be observed after 1 to 1-1/2 years of age. In some larger breeds, puberal estrus may not occur until nearly 2 years of age. If these bitches are truly anestrus, the ovaries and reproductive tract are small, hypoplastic and juvenile. Delayed puberal estrus may be due to nutritional deficiencies, stress of disease and environmental and husbandry conditions. Failure to observe puberal estrus can also be due to a "silent" estrus or shallow estrus. These are characterized by minimal to no vulval discharge and/or vulvar size change and poor attraction of males, but ovulation and mestestrus/diestrus are followed by normal anestrus and normal behavior and expression of estrus in the second heat.

Vaginal cytology and blood progesterone levels are helpful in detecting the metestrus/diestrus period fol-

lowing an undetected estrus. Failure to cycle is also associated with hypothyroidism, primary ovarian or adrenal dysfunction, intersexuality, or a previous unreported ovariectomy. These conditions should be ruled out by blood tests for hypothyroidism, adrenal cortical function and sex steroid levels, physical examination, evidence of clitoral enlargement, vaginal abnormalities and scars of a possible previous ovariectomy. Sex chromosome or karyotypic analysis in suspected intersexes is also diagnostic.^{143,148,160,206,212}

Anestrus can be seen in bitches that have had previous estrous cycles or pregnancies, and currently have an abnormal long interestrus interval. Most breeds will recycle in 8 months. Some breeds, such as the Basenji, wolf and coyote crosses, usually have only one cycle a year. It is the author's experience that frequently "so called" anestrus bitches have been missed and can be in metestrus. Many are hypothyroid. Vaginal cytology, progesterone determination for the metestrus/diestrus state and a TSH response test for hypothyroidism are used to determine these conditions. It is also important to know the use of these bitches. If their environment and handling are stressful, such as intensive training, performances, working, showing, endurance racing, and Greyhound racing, it will cause certain individuals to delay or interrupt cycles. These animals need to be changed into a less stressful handling and a more stable environment before cycles will return.

True anestrus bitches with no obvious reason for delay of treatment can be induced into estrus (See section on induced estrus in canine physiology). The author's best clinical results follow the administration of 25 mg of FSH-P subcutaneously every 7th day for 5 weeks, and weekly vaginal cytology examinations prior to the next injection to detect proestrus changes.¹⁵ Many bitches will show proestrus between the second and third injections. When signs of proestrus are seen, a daily vaginal cytology examination is performed with breeding taking place during maximum cornification. The bitch should be bred at least 2 or 3 times at 48 hour intervals. If vaginal cornification is not complete and progressive and vaginal cytology indicates a return to anestrus, daily injections of FSH-P starting with 25 mg, 15 mg and 5 mg on successive days, and monitored daily with vaginal cytology are instituted. Usually 75 to 100 percent of the vaginal cells will be cornified and anuclear on the 3rd day of this therapy. At this time, 250 to 1000 units of HCG is administered intramuscularly and the bitch is bred. Ten days following the last breeding, blood progesterone levels are checked. Levels over 20 ng/ml are normal and indicate adequate ovulation and luteal formation. Levels between 10 to 20 ng/ml indicate ovu-

lation, but less luteal tissue, a lower number of ovulations, decreased luteal function, or delayed ovulation. Levels lower than 5 ng/ml or at the baseline of anestrus indicate no ovulations with atresia of follicles, luteal cysts or delayed ovulation. When low levels are encountered, another progesterone blood level should be determined at the time of pregnancy palpation or ultrasound pregnancy check at 25 to 30 days to determine if levels have reached maximum indicating delayed ovulation or no ovulation if progesterone levels are still low and pregnancy has not occurred. If after 5 weeks of FSH, no proestrus signs are evident, the bitch should be given no treatments for 4 to 6 weeks, but watched carefully for proestrus and if still anestrus following this period FSH therapy should be repeated weekly for another 5 weeks.

Short interestrus intervals are those seen in bitches that have less than 4 to 4-1/2 month intervals from one proestrus to the next. In the Beagle, approximately 150 days is needed for completion of endometrial desquamation and repair after the onset of estrus. Bitches with short interestrus intervals are frequently infertile. Possibly this infertility is caused by implantation failure, failure to ovulate or poor luteal formation and longevity. Progesterone blood levels should be performed during metestrus to determine if maximal ovulation and luteal formation have taken place. A suggested treatment is to place the bitch on a contraceptive such as mibolerone (Cheques, Upjohn Co.) and suppress the next several estrous cycles until breeding is desired and then breed on the next estrus after removal of the daily oral contraceptives.^{143,148}

Occasionally a bitch may have "split" or "false" estrus which will be characterized by vulvar swelling, blood-tinged proestrual discharges, attraction of males, a proestrus vaginal cytology followed by a return to anestrus and a quiescence of 2 to 6 weeks or longer until the bitch has another false or a full estrous cycle. This is seen in the puberal as well as later estrous cycles and can be seen when environmental changes are upsetting, e.g., shipping to breeders, infectious disease outbreak, training, endurance racing, etc. These bitches are usually fertile once they accomplish a normal estrus.

Some bitches fail to show standing behavioral estrus, but undergo full vaginal epithelial cornification with ovulation. This occurs in bitches with vaginal/vestibular strictures or with bitches that object to a particular male or any male. Breeding with restraint and muzzling or artificial insemination and use of vaginal cytology and/or vaginal mucosal changes to determine the onset of estrus usually results in pregnancy. This type of bitch can be the highly cuddled household dog that is socialized to humans but not other dogs, shy bitches, or a bitch

with a vicious attitude towards any other dog.

Occasionally a bitch will display a **prolonged estrous standing behavior** for any male, usually longer than 10 days and possibly into mid-metestrus/diestrus and pregnancy. Delayed ovulation, failure to ovulate or cystic follicular degeneration are possible causes of this behavior. Vaginal cytology and progesterone blood levels should be used to determine if the bitch is still in a proestrous or estrous stage. Many bitches will have normal metestrus/diestrus vaginal cytology, adequate progesterone blood serum levels (over 20 ng/ml) and be pregnant, but still accept the stud dog. Once the vaginal cytology changes from maximum cornification to less cornification, breeding should be stopped.

The queen is a seasonal breeder and responds to an increase in daylight or artificial light. Puberal estrus may be seen as early as 4 months of age in the early spring-born kitten that is well-grown, disease-free or may not occur for 12 months in the late spring, summer or fall-born kittens. **Anestrus**, like in the bitch, is associated with nutritional and disease states, gonadal hypoplasia, intersexuality, environmental stresses and also in the queen, the effect of insufficient light.^{121,167,239} Secluded house queens that select dark areas may never come into estrus. Also, single housed queens are less likely to show estrus compared to socialized queens housed with other cycling queens or tom cats.^{43,121,167} True anestrus queens are successfully induced with PMSG or FSH regimens (see section on estrus induction in feline physiology). Hypothyroidism is uncommon in the cat and is seldom a cause of anestrus.

Nymphomania in the bitch is characterized by excessive sexual desire and hyperestrogenism. Occasionally a bitch will mount and ride males, but not permit copulation. This condition may be caused by single or multiple follicular cysts or by functional granulosa cell tumors producing estrogens. These bitches are usually infertile with endometrial cystic hyperplasia caused by prolonged estrogen or estrogen/progesterone stimulation. Several early workers reported follicular and luteal cysts in older dogs and cats.^{25,86,175,176,177} Anderson and Simpson identified only 7 (3%) follicular cysts in ovaries in their aging Beagle study.⁶ None of these bitches showed clinical signs of nymphomania. Epithelial tubule proliferation or subepithelial structures, granulosa cell and rete ovarii derived cysts were most frequently found in their study.

The pathogenesis of follicular cystic degeneration in the dog is not known, but is probably similar to cattle. Hyperestrogenism is characterized by vulvar swelling, vulvar discharge, cystic endometrial hyperplasia, mammary gland hyperplasia, endometritis and pyometritis and

genital tract fibroleiomyomas or fibroids. Functional luteal cysts may cause increased progesterone blood levels which frequently lead to cystic endometrial hyperplasia-endometritis-pyometritis complex. These individual cases need more clinical documentation, e.g., vaginal cytology, vaginoscopic and laparoscopic studies, sex steroid hormone blood levels, and sex behavioral studies.

Queens with cystic follicular degeneration usually show signs of nymphomania, attract tom cats and show signs of proestrus but will not allow mating. Many are ill-tempered and unsuitable for pets during this time. The most frequent ovarian cyst in the cat at any age is cystic rete ovarii. These queens do not show nymphomania. These are found in queens at any age and can cause complete destruction of the ovary resulting in a cystadenoma. Nymphomania in the queen should not be misdiagnosed in cats with regular cycles that are not mated or receive only a single mating with insufficient vaginal stimulation to cause ovulation. These queens may remain in estrus for 10 to 20 days or longer and return in a few days to a few weeks with a similar cycle. Queens that have a sterile mating and ovulate will have a pseudopregnancy of 20 to 45 days and again return to proestrus and estrus within 7 to 14 days during the breeding season. These queens will respond to breeding and are usually fertile. Exogenous HCG, 25 to 200 units, intramuscularly given once or adequate pseudocopulation will cause the queen to ovulate and become pseudopregnant.

Treatment for bitches and queens with cystic follicular degeneration is designed to attempt luteinization of the cyst or ovulation with exogenous HCG given intramuscularly at a dose of 100 to 1000 units or the use of progestins to counteract hyperestrogenism. Progestins may result in further endometrial hyperplasia, endometritis and pyometritis. Once a regular cycle is produced, these animals should be bred. If litters are not desired, these animals are best treated by ovariohysterectomy.

Hyperestrogenism and nymphomania can be seen in spayed bitches and queens. This is usually due to an ovarian remnant or possibly accessory ovarian tissue between the removed ovary and the attachment of the ovarian ligament to the body wall.²⁰⁹ A laparoscopic examination, identification and removal of the remnant is best accomplished when the animal is showing signs of estrus and the vaginal cytology is cornified. At this time the follicles or cysts are present making the remnant easier to identify. Injection of HCG, 100 to 1000 units, once, intramuscularly, may cause ovulation and/or lutenization with increased progesterone blood levels, but in time these animals will recycle. Removed ovarian remnants should be checked by histopathology to identify ovarian structures. Hyperestrogenism in either queens or bitches

may lead to estrogen toxicity, bone marrow depression, thrombocytopenia, and rapid hemorrhagic shock and death.²⁴⁰

Spayed or intact bitches may attract males because of vaginitis, vestibulitis, or clitoritis but not accept copulation. Metritis, endometritis, uterine tumors, even in spayed bitches that did not receive a total hysterectomy, and possibly infected anal glands, may be other causes of "constant" attraction of males. It appears that these conditions cause the release of the sex pheromones from the vulva and vestibule. In spayed bitches, uterine stump infections or abscesses will cause vaginitis, vaginal discharge and attraction of males. Removal of these conditions by surgery or medical treatment will resolve the problem. Any vulvar discharge must be diagnosed by vaginal and vulvar culture, cytology, vaginoscopic and possibly laparoscopic examination. Intersexes with active ovarian tissue or abdominal testicles with Sertoli cell tumors producing estrogens will cause hyperestrogenism and attraction of males. Diagnosis of intersexes followed by gonadectomy will correct this condition.

Sterility caused by insufficient secretion of progesterone or hypoluteoidism in either queens or bitches must be well-documented by repeated embryo or fetal loss or abortion at the same stage of pregnancy. All other causes such as infectious diseases, low grade reproductive tract infections or degenerative endometrial conditions, and genetic causes must be differentiated. Blood progesterone levels taken bi-weekly are helpful in diagnosing hypoluteoidism. Repositol progesterone, 0.25 to 0.5 mg/kg, intramuscularly, at weekly intervals, starting 7 to 10 days before the expected abortion and terminated 7 to 10 days before expected parturition has been used successfully in the queen.¹²¹ Progesterone administered to the bitch during pregnancy can lead to intersexuality in female pups resulting in female pseudohermaphrodites.²⁵¹

Pseudopregnancy or pseudocyesis (false pregnancy) in bred or unbred bitches produces typical maternal behavior and signs at the approximate time of normal parturition along with mammary gland development and even the production of milk. Lactation may persist for 2 or more weeks and is encouraged by nursing or adoption of unrelated neonates and inanimate objects. The bitch may show nesting, mothering activity, restlessness, irritability, anorexia, and false labor. The abdomen may be distended and the uterus is palpable and shows endometrial hyperplasia grossly and/or microscopically. Vomiting, diarrhea, polyuria, polydipsia, and polyphagia have all been reported. Pseudopregnancy can be both "overt" or "covert." All dogs that ovulate undergo a physiological pseudopregnancy, but some individuals

will show behavioral signs.^{144,146,247} There is no correlation between expression of pseudopregnancy and reproductive disease or fertility.

Pseudopregnancy is caused by the decrease of progesterone following luteolysis and the pituitary release of prolactin as progesterone levels fall. Prolactin release can be enhanced by nursing and the presence of the neonates. In some bitches, ovariohysterectomy during the metestrus/diestrus state of pregnancy will result in prolactin release and "overt" signs of pseudopregnancy. Others, following progestin therapy, such as megestrol acetate (**Ovaban-Schering**) will respond with increased prolactin levels and overt signs of pseudopregnancy.^{144,146}

Pseudopregnant bitches should be treated with supportive therapy such as care of the mammary gland and sedation if needed for psychological and behavioral changes. Treatment with any of the sex steroids will mediate negative feed-back and inhibition effects on the hypothalamic-pituitary axis.⁹ Androgens, such as testosterone at 1 to 2 mg/kg once intramuscularly, or mibolerone (**Cheques-Upjohn Co.**) given orally to effect are preferred. Megestrol acetate, 2 mg/kg, orally, once daily for 8 days is very effective, but relapse following therapy will occur in some bitches. Bromoergocryptine is highly effective in reducing prolactin secretion, but the human drug forms have severe side effects and depressive behavioral actions on the bitch. A new bromoergocryptine product has been developed in Europe for use in the dog and is reported to be very successful but is not available in the United States.^{138,183}

The queen in the absence of coitus usually has no luteal phase. A few queens can be stimulated to ovulate by stroking the perineum or handling and will spontaneously ovulate.⁸⁷ If a sterile mating occurs, or ovulation is induced by exogenous LH, or vaginal stimulation with a probe, corpora lutea are formed and a pseudopregnancy occurs but is less persistent than in the bitch, with luteolysis taking place in 20 to 45 days.

Very few queens show "overt" pseudopregnancy. Occasionally there will be mammary gland engorgement, queens may allow young to suckle or display parturient behavior and maternal behavior towards inanimate objects. Usually no treatment is necessary. If therapy is indicated, repositol testosterone (1 mg/lb) or tranquilization may be provided.²³⁹

Preventing conception in mismating in bitches and queens has been discussed previously in the sections on Canine and Feline Physiology and is usually accomplished with estradiol cypionate injected in the first 5 days following breeding or during true estrus or late estrus. Administration during proestrus may not prevent

conception. Usually .25 mg to 2 mg, intramuscularly are the dose ranges. Several side effects, such as prolonged estrous behavior, pyometritis and estrogen bone marrow depression are undesirable. Other methods include the use of diethylstilbesterol tablets and several abortifacient drugs such as prostaglandins and their analogs, and bromocryptine drugs, which are undergoing experimental studies at this time, but offer potential alternatives (see sections on Canine and Feline Physiology).

Incontinence of urine following ovariohysterectomy in bitches is still poorly understood. There appears to be no age or breed predisposition and in general, for the number of ovariohysterectomies done in this country it is not a common sequela. The condition is infrequently reported in the queen. In one study, in dogs, the mean age of occurrence was 8.3 years (range 1 to 15 years).²⁰³ In some, the condition was seen most frequently when disorders causing polyuria developed. The diagnosis is made after differentiating neurogenic from non-neurogenic incontinence.^{197,203} This condition is usually diagnosed after other causes of urinary incontinence such as ectopic ureters, patent urachus, pseudohermaphroditism, urethrectal fistulas, obstructive incontinence and others are ruled out. Diagnosis is made by remission of urinary incontinence following estrogen therapy. Oral administration of 0.1 to 1.0 mg/day of diethylstilbesterol for 3 to 5 days followed by a maintenance dosage of approximately 1.0 mg/week is needed. Another treatment is 0.1 to 1.0 mg of estradiol cypionate, intramuscularly administered at intervals of weeks to months. These are completely empirical doses. The lowest dosage should be used because of the myelotoxicity of estrogen therapy in dogs. Recent experiments in rabbits show that ovariectomy decreases sensitivity to stimulation of alpha adrenergic receptors in the bladder and urethra that are important in controlling incontinence and that these receptors are estrogen sensitive.²⁰³ Adhesions between the stump of the uterus and the bladder, urethra and ureters following ovariohysterectomy may also result in urinary incontinence.^{25,195,203}

Hyperadrenocorticism in the dog of either sex is occasionally observed and can be caused by tumors of the pituitary gland or hypothalamus.¹²⁹ The most frequent primary pituitary neoplasm in the dog is the chromophobe adenoma.^{150,153} These tumors usually secrete excess adrenocorticotrophic hormone (ACTH) which results in hyperadrenocorticism. Other causes are functional adrenocortical tumors, abnormal negative feedback mechanism and iatrogenic causes.²¹¹ Iatrogenic canine Cushing's syndrome is due to exogenous glucocorticosteroids, which suppress endogenous ACTH secretion, causes atrophy of the zona fasciculata resulting in re-

duced endogenous glucocorticoid production and secretion. The iatrogenic form has been seen both in dogs and cats where prolonged and excessive use of glucocorticosteroids, and progestins such as megestrol acetate (**Ovaban**) administered for skin conditions, urine spraying in tom cats, aggressiveness or prolonged suppression of estrus.

This condition usually develops in dogs 5 years old or older. Purebred dogs, especially Miniature and Toy Poodles, Dachshunds, and Boston Terriers are most commonly affected, although any breed or mixed breeds can develop this condition. Primary hyperadrenocorticism is rare in cats. Clinical signs include bilateral symmetric alopecia, dull, dry and easily epilated hair, dermal atrophy, variable hyperpigmentation, muscle weakness, pendulous abdomen due to muscular weakness and hepatomegaly. Females are usually anestrus and 20 to 30 percent have an enlarged clitoris suggesting excessive androgens. Testicular atrophy is found in approximately 30 percent of the affected male dogs.²¹¹ In dogs with pituitary tumors, there is usually diabetes insipidus with polyuria, polydipsia and polyphagia. These dogs are usually hypothyroid, which also contributes to skin disorders and infertility and results in a lowered basal metabolism. In another study of this condition, clinical signs and prevalence were listed as polyuria and polydipsia in approximately 85 percent of cases, abdominal distension, 75 percent, anestrus, 70 percent, polyphagia 70 percent, muscular weakness and atrophy, 50 percent, bilateral symmetrical alopecia, 40 percent, testicular atrophy, 40 percent, comedones, 35 percent and calcinosis cutis, 10 percent.²⁰⁵

Laboratory tests for diagnosis include increased blood cortisol levels, absolute lymphopenia, eosinopenia, low urine specific gravity, low thyroid function test, hypercholesterolemia, and elevated serum alkaline phosphatase level (liver dysfunction). The more definitive tests are the ACTH response or a dexamethasone-suppression/ACTH-stimulation test.^{205,212} A high-dose (0.1 mg/kg) dexamethasone suppression test can more definitively diagnose either pituitary-dependent Cushing's syndrome with depressed serum cortisol from a functional adrenal tumor which does not depress serum cortisol. Whereas the low-dose (0.015 mg/kg) test is a screening test for a normal dog.²⁰⁵

Treatment consists of administering o,p'-DDD (**Lysodren**, Bristol Laboratories, Syracuse, NY) an analog of DDT, a drug that selectively causes necrosis of the zona fasciculata and reticularis. The initial dose is 50 mg/kg daily for 10 days with glucocorticoid supplementation; prednisolone, 0.2 to 0.4 mg/kg daily or cortisone, 1 to 2 mg/kg daily, to reduce the side-effect of

acute cortisol withdrawal from necrosis of the adrenal cortex.^{205,211} Surgical bilateral adrenalectomy and/or hypophysectomy can also be therapeutic, but skillful surgery, intensive monitoring and lifelong hormone replacement are required.

Pituitary dwarfism in dogs has been described in German Shepherds and Karelian Bear dogs.¹⁵⁰ It is a genetic disease caused by a recessive autosomal gene. Affected puppies are normal at birth but grow at a much slower rate than normal litter mates due to a deficiency of somatomedin, a growth promoting protein which is stimulated by growth hormone or somatotrophin (STH). These dogs keep their puppy hair for months and fail to develop sexually.^{150,229}

Pituitary cysts or other abnormalities may result in loss of sexual function. Cysts or abnormalities of the craniopharyngeal duct or Rathke's cleft are common in dogs. Depending on size, location and number of cysts, pressure on the neurohypophysis resulting in its destruction, may cause dwarfism, diabetes insipidus, genital atrophy, and obesity.^{150,153} Parasitic migration, usually of larval forms, may lead to massive pituitary destruction and inflammation resulting in hypopituitary function.¹⁶⁸

Acromegaly is caused by hypersecretion of growth hormone in the mature animal. It has been reported in dogs associated with injections of anterior pituitary gland extracts, eosinophilic cell hyperplasia of the anterior pituitary gland, administration of progestational compounds and in some intact bitches following the progesterone normally produced during metestrus/diestrus.^{64,89,187,229} Canine acromegaly and mammary gland nodules were reported following the administration of medroxyprogesterone acetate (MPA).⁶⁴ Canine acromegaly is characterized by inspiratory stridor due to diffuse soft tissue increase in the orolingual/oropharyngeal region, thick skin caused by myxedematous skin developing excessive folds, hypertrichosis, abdominal enlargement, diabetes mellitus, polyuria-polydypsia and fatigue. The dog appears to be particularly sensitive to the diabetogenic action of growth hormone which is characterized by hyperinsulinemia followed by hypoinsulinemia and exhaustion or pancreatic B-cells.⁸⁹ Dogs with acromegaly have elevated growth hormone plasma levels (11 to 1476 mg/ml). Dogs with acromegaly and diabetes associated with diestrus or progestational compounds that were administered respond well to ovariectomy or removal of the progesterone therapy, respectively.^{64,229}

Hypoestrogenism as a cause of an estrogen-responsive dermatosis, is a rare bilateral alopecia, seen in spayed female dogs. The cause and pathogenesis is not known. The condition is seen in spayed bitches and believed to

be seen more frequently in prematurely ovariohysterectomized dogs. In affected dogs it is hypothesized that the adrenal cortex may not produce sufficient estrogens.¹⁸⁷ Diagnosis is based on history, physical examination, laboratory elimination of other endocrine skin diseases such as hypothyroidism and hyperadrenocorticism and responsive therapy consisting of 0.1 to 1.0 mg of diethylstilbesterol orally, once daily and continued on a three weeks "on" and one week "off" basis until hair growth is evident. If good response is not seen in three months, the diagnosis is questionable. When good response is seen, a maintenance dose of 0.1 to 1 mg given once or twice weekly is established. If signs of estrus occurs, the dose should be lowered. Estrogen-induced bone marrow depression (thrombocytopenia, leukopenia, anemia) must be monitored by hematological examination.²⁴⁰

Hyperestrogenism caused by follicular cystic degeneration, functional granulosa cell tumor, Sertoli cell tumor in pseudohermaphroditism, or prolonged administration of large doses of estrogen may cause **alopecia**. The alopecia begins in the perineal and genital regions and may eventually involve the ventral abdomen and chest, flanks and neck. The skin can be thin or of normal thickness. The hair is easily epilated. These animals usually attract males, can have gynecomastia, usually have a vulvar discharge, an estrous type of vaginal cytology with cornification and frequently develop cystic endometrial hyperplasia-endometritis-pyometritis complex.⁸⁵

Hypothyroidism is the most common endocrine disorder of the dog. In a study of 2033 T₄ determinations of suspected hypothyroidism cases an incidence of 9.4 to 36.6 percent among 15 breeds of dogs was found;^{23a} Schnauzers, 9.4%, Dachshund, 10.5%, Chihuahua, 16.3%, Poodle, 18.2%, Doberman, 19.4%, Shepherd, 19.6%, Setter, 20.3%, Mixed, 20.5%, Collie, 21.2%, Terrier, 21.9%, Spaniel, 22.6%, Retriever, 23.5%, Labrador, 31.1%, Sled Dog, 33.3%, Beagle, 36.7%. Another study showed a relative risk factor of Chow Chow, 11, Great Dane, 4.1, Irish Wolfhound 4.1, Boxer, 7.8, English Bulldog, 3.2, Dachshund, 2.8, Afghan Hound, 2.7, Newfoundland, 2.6, Malamute, 2.5, Doberman Pinscher, 2.2, Brittany Spaniel, 2.0, Poodle, 2.0, Golden Retriever, 2.0 and Miniature Schnauzer, 2.0. A reduced risk was found for Beagle, Cocker Spaniel, English Springer Spaniel, German Shepherd and the mongrel.¹⁸⁷ These results are conflicting. Genetic studies concerning hereditary hypothyroidism are lacking. The two main causes of hypothyroidism in dogs are lymphocytic thyroiditis, an autoimmune disease, and idiopathic thyroid necrosis and atrophy. Secondary hypothyroidism, seen in about 10% of the cases is associated with pituitary

dwarfism and pituitary neoplasia.¹⁸⁷ There is no sex predilection for canine hypothyroidism and dogs between the age of 6 to 10 years are most often affected. Larger and giant breeds usually are affected at an earlier age of 2–3 years.

Associated reproductive abnormalities in the bitch include general infertility, prolonged interestrual periods, anestrus, prolonged estrous bleeding, shallow estrus, and short cycles.¹⁰⁰ In the male, abnormalities include poor libido, testicular atrophy and oligospermia. Other clinical signs include a wide range of dermatologic signs including a dry and brittle coat, patchy alopecia over points of wear, easy epilated hair, poor hair growth after clipping, poor hair turnover in cheek and temporal regions of short-haired dogs and a fine puppy-like coat in long-coat breeds. The skin is often dry, scaly, thickened and may appear myxedematous, especially facial skin. All forms of seborrhea and pyoderma can occur secondarily.

Other clinical signs can include mental dullness, lethargy, fatigue, obesity, hypothermia with desire to seek warm, heated places, cardiovascular signs including bradycardia, weak apex beat and decreased amplitude of QRS complex in all EKG leads. Cardiac dysrhythmias with congestive heart failure and myocardial changes are seen in largebreed dogs. Musculoskeletal/neurologic symptoms can be seen with severe hypothyroidism and include weakness, limb stiffness and dragging or knuckling of the feet. Clinicopathologic abnormalities include mild to moderate normocytes, normochromic anemia, serum lipid abnormalities, fasting lipemia, hypercholesterolemia and hypertriglyceridemia.^{187,219} In the author's experience, many bitches may be subclinically hypothyroid and show no other clinical signs than infertility.

Diagnosis of hypothyroidism is best performed by the thyroid stimulating hormone (TSH) response test. One procedure is to collect pre-injection baseline blood samples, inject 5 IU of TSH intravenously, and collect a post-injection blood sample 4 hours later. The baseline plasma level of T_4 is between 1.5 and 3.0 ug/dl; T_3 is between 1.0 and 2.0 ng/ml.²¹² Four hours post TSH stimulation, the T_4 and T_3 levels are increased 2 to 3 times. Dogs with primary and secondary hypothyroidism have subnormal or low normal baseline levels of T_4 and very little change after TSH stimulation. Baseline and post TSH; T_3 are more variable and less predictable. Normal levels of T_3 and T_4 and TSH response test can be different from laboratory to laboratory and should be checked for interpretation of results.

Treatment with thyroid replacement therapy is very beneficial and the clinical states usually return to normal. Synthetic products include L-thyroxine (T_4) called **Levothyroxine**, given orally at 20–32 ug/kg daily or

20 ug/kg every 12 hours in smaller dogs; L-triiodothyronine (T_3) called **Liothyronine**, is administered orally at 4.4 ug/kg every 8 hours; or L-thyroxine and L-triiodothyronine combined ($T_4 - T_3$) called **Liotrix**, administered at 20 ug/kg T_4 , 5 ug/kg T_3 every 12 hours and crude desiccated thyroid thyroglobulin, given orally at 15–20 mg/kg, once daily or divided every 12 hours. Post treatment testing after 4 to 6 weeks is indicated about 4–8 hours after an oral treatment to check for adequate replacement levels.²¹⁹

Clinical spontaneous hypothyroidism in the cat is unknown. Hyperestrogenism and hypoestrogenism as seen in the bitch can be seen in the queen.

Pathology of the Genital Tract

The principle pathology of the genital tract in the bitch and queen are developmental anomalies, cystic embryological remnants, hyperplastic and degenerative changes, neoplasia, inflammation and infection.

Developmental Anomalies and Cystic Embryological Remnants

In the study by Anderson and Simpson, ovarian cysts increased with age in the Beagle bitch and originated from follicles, corpora lutea and epithelial tubules (subsurface epithelial structures, SES), granulosa cell cords, rete ovarii and remnants of the mesonephric (Wolffian duct) or paramesonephric (Mullerian duct) ducts (paraovarian cysts).⁶ Follicular cysts, luteal cysts, and cystic corpora lutea were less common than epithelial tubular cysts and were not correlated with endometrial changes or nymphomania.⁶ Luteinized cystic follicles occur more frequently than cystic follicles.¹⁷⁶ Epithelial tubular cysts, also called subsurface epithelial structures (SES) are frequently multiple and are located in the cortex from the downgrowth of surface epithelium. Epithelial cysts may also be seen in the medulla or hilus. They are usually lined by simple epithelium. The epithelium may proliferate and become papillary. This hyperplastic condition may proliferate and eventually result in ovarian cystadenocarcinoma. Surface epithelium of the ovary becomes increasingly more active with advancing age in man, rodent and dog.⁶ In aged bitches the cortex may be replaced by multiple epithelial tubules and cysts resulting in complete destruction of the germinal cortical tissue. These bitches are anestrus. The cysts contain a clear watery secretion with little protein content which will remain fluid when fixed with formalin fixative, com-

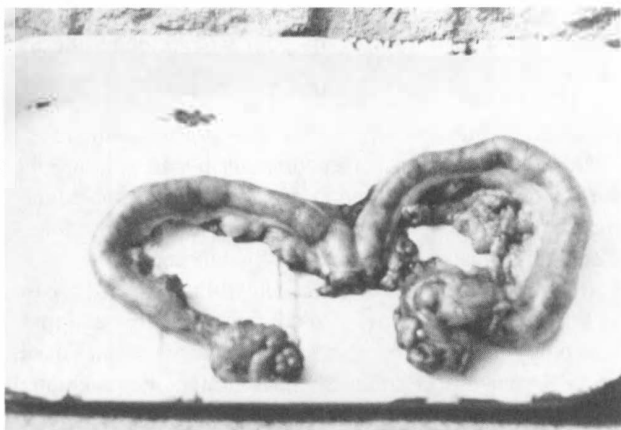


Figure 152 Pyometra in a Bitch (Pseudomonas organisms were recovered from the uterus of the ill 8-year-old female)

pared to follicular or luteal cysts which contain an amber fluid rich in protein that will become solid and amorphous with formalin fixation.

In the aging Beagle bitch, granulosa cell cords (sex, egg or ova cords) can equal or exceed the number of epithelial tubules, whereas in the young adult, the ratio of epithelial tubules to granulosa cell cords was 4:1. These tubules develop from atretic follicles and remnants of the original migrating granulosa cell cords.^{6,241} Granulosa cell

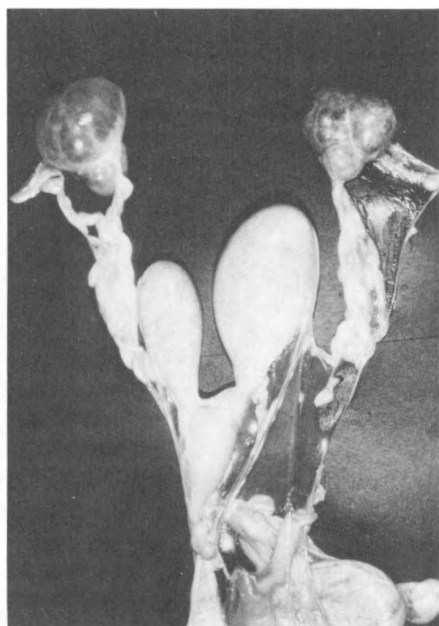


Figure 153 Segmental Aplasia of the Uterine Horns with Mucometra in a Bitch. (Courtesy K. McEntee)

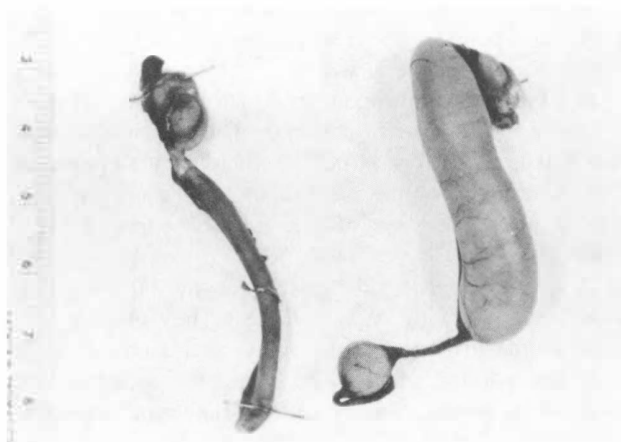


Figure 154 Segmental Aplasia of the Right Uterine Horn with Mucometra in a Queen. (Courtesy K. McEntee)

cords are the precursors of the granulosa cell tumors, pseudotesticular tubules, sex cord stromal tumors, androblastoma, arrhenoblastoma or Sertoli-Leydig cell tumors of the ovary of the dog and cat. Granulosa cell cords are most frequently found near the corticomedullary junction but may occur in any region of the ovary.

The rete ovarii located in the hilus of the ovary in 10% of Beagles over 8 years of age contain cysts of variable size, while in another 5%, the structure was greatly enlarged.⁶ Hyperplasia with papillary proliferation occurs with age and in some bitches, the proliferation of epithelial, granulosa cell cords and hyperplastic tubules of the rete are difficult to distinguish apart.⁶ A large parovarian cyst was diagnosed following an ovariohysterectomy in a 7-year old West Highland White terrier.⁹³ A large ovarian cyst (19 × 7 cm) was grossly diagnosed

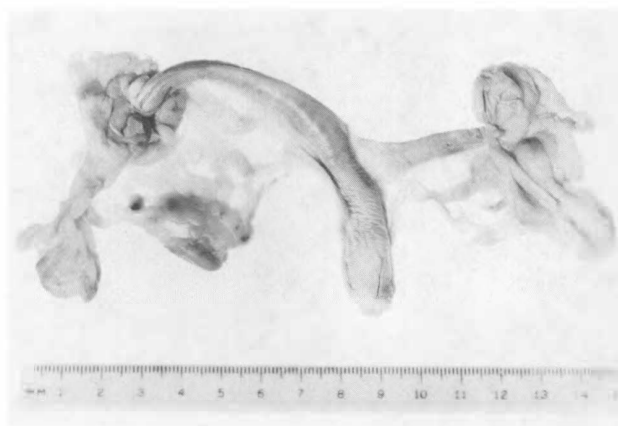


Figure 155 Uterus Unicornis in a Bitch (Courtesy J. D. Sweet)

as a functional follicular cyst because the 11-year old Labrador Retriever that it was removed from had a persistent estrus for several weeks.^{219a} The cyst and ovaries of this bitch were not examined histologically. Thus it is impossible to classify this cyst. The size would indicate that it possibly was not a follicular cyst but either a parovarian cyst of mesonephric or paramesonephric origin or a cystadenoma of one of the ovarian tubular structures. (See Figures 156–158)

Cystic rete ovarii in the queen become large enough to be confused with cystic follicles. They may be singular and destroy most of the ovary. Frequently they are incidentally found, and may be seen in the young as well as the older queens. The cyst if non-functional, contains clear watery fluid with little protein compared to the amber protein-rich fluid of follicular or luteal cyst. Follicular cystic degeneration has been reported in the queen.^{175,239}

Anderson and Simpson reported in aging Beagles that small cysts occurred in the fimbria and proximal portion of the oviduct, some obtaining the size of 1 cm in diameter. Fibrosis of the middle and distal portion of the oviduct was observed. Beagles between 4 and 8 years of age had uterine abnormalities that could impair their ability to reproduce. At ages between 9 and 17 years, two-thirds of the dogs had prominent uterine pathology. Hyperplasia of the endometrium was characterized by proliferation of glands, cystic formation and formation of variable-sized folds extending into the lumen of the uterus. Fluid accumulation either as hydrometra, mucometra, or pyometra was present in some. Approximately 4% of 216 Beagles developed moderate to severe pyometra. Beagles with cystic hyperplasia-pyometra syndrome usu-

ally had corpora lutea present. Atrophy of the endometrium was characterized by poorly developed uterine glands and a dense lamina propria.⁶ Further discussion on the cystic endometrial hyperplasia, endometritis, pyometra syndrome will occur later in this chapter.

Other complications of endometrial hyperplasia are the formation of pedunculated cystic endometrial polyps that may be singular or multiple and attain the size of a fetus. The author has seen pedunculated endometrial polyps in both aged bitches and queens. The author studied a case of torsion of one uterine horn containing a large endometrial polyp resulting in rapid hemorrhagic shock and death in an 8-year old German Shepherd bitch. Pedunculated endometrial polyps can prolapse through the cervix and result in a constant bloody and fetid vulvar discharge.

Another sequela of endometrial hyperplasia is adenomyosis, a downgrowth of hyperplastic glands into the myometrium. These masses are frequently misdiagnosed as a leiomyoma or fibroids until sectioned and the glandular “swiss cheese” muscle is noted.

Firm vaginal polyps were reported in 25% of Beagles over 10 years of age. These polyps can prolapse through the vulva.⁶

Segmental vaginal aplasia with incomplete development of the Mullerian duct was reported in 3 Beagles.²⁴⁸ Persistence of the mesonephric duct just lateral to the uterus and cervix in the broad ligament or the ventral floor of the vagina may be found as single or multiple cysts, tubules or the entire duct either unilaterally, but more frequently bilaterally. A persistent post-cervical band caused a dystocia in a 19-month old nulliparous Bull Terrier.¹²⁰ Congenital vestibulo-vaginal stenosis has been reported in several bitches. One study reported on

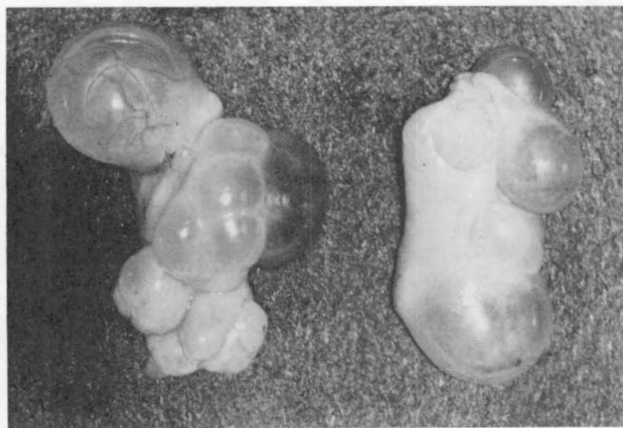


Figure 156 Cystic Ovaries from a Bitch
 (Courtesy K. McEntee)

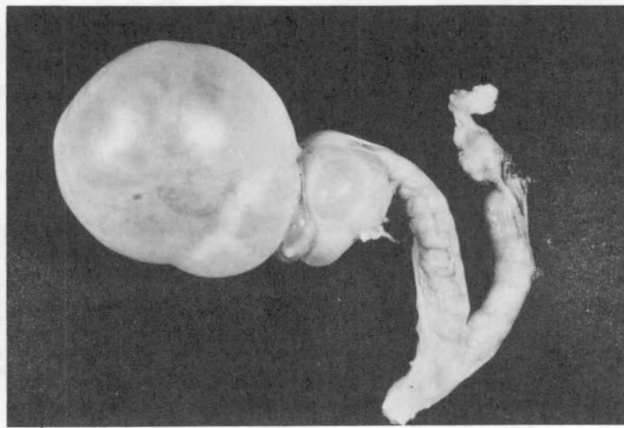


Figure 157 Cystadenoma of a Feline Ovary
 (Courtesy K. McEntee)

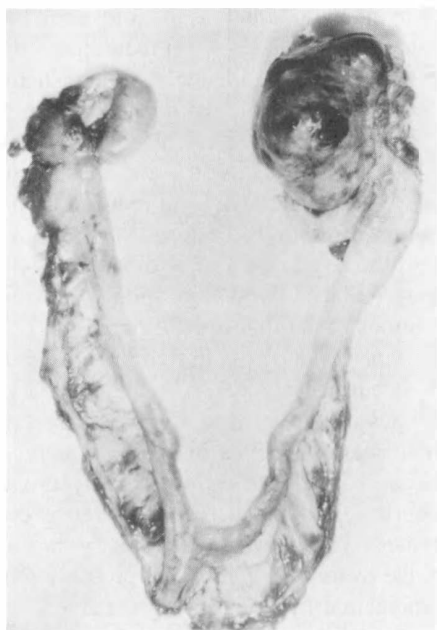


Figure 158 Granulosa Cell Tumor of a Canine Ovary
(Courtesy K. McEntee)

22 maiden bitches, 13 with strictures and 9 with persistent but perforate hymens. These bitches showed vulvar pruritus, incontinence, increased micturition frequency, vestibulitis and vaginal inflammation and mating difficulties, usually refusing copulation.¹²⁷ Diagnosis is made by digital examination, vaginoscopy, or radiography with pyelography or pneumocystography. Surgical correction is possible and sometimes necessary if constant irritation or chronic inflammation is present. In breeding bitches, artificial insemination with resulting pregnancy usually leads to a normal uncomplicated pregnancy and correction of the condition. If delivery is difficult, then an episiotomy at 11 or 2 o'clock position or a Caesarian section will alleviate the dystocia. In the author's experience, this condition is probably inherited and is seen frequently in the German Shepherd breed. Multiple fibrotic stenotic rings may be present cranially from the vestibulo-vaginal junction. The rings in the mid-vaginal area may create a "dam" that affects the flow of vaginal and uterine discharges resulting in periodic drainage of mucoid, serous or purulent debris and attraction of male dogs. A 3-month old German Shepherd with a congenital mid-perineal vulvo-vaginal cleft was repaired surgically with a good cosmetic effect.⁴⁵ The author has seen this condition in other German Shepherds and other large breeds of dogs. Other defects are the small juvenile vulva or the dorsal vulvar fold that covers a deep-seated, slightly tipped or inverted vulva.

Vaginal prolapse is seen in some dogs during increased endogenous estrogen levels of proestrus and just prior to whelping and is frequently called vaginal eversion or vaginal hypertrophy.²²⁰ This condition is seen frequently in the Bull Mastiff and Boxer breeds and is considered an inherited syndrome. Most bitches in proestrus will display a slight hypertrophy of the floor of the vagina and vestibule, but in some, it is so exaggerated that a protruding symmetrical mass will prolapse over the urethral meatus and occasionally the entire circumference of the vagina will prolapse resulting in a doughnut-shaped mass. The tissue is hypertrophied and edematous. This condition must be differentiated from a vulvo-vaginal leiomyoma, fibroid or polyps or a transmissible venereal tumor. The stage of cycle, symmetry and examination will differentiate vaginal prolapse from the above conditions. Severe cases must be artificially bred to become pregnant. This condition is inherited and the author has seen kennels where every bitch is affected. The condition will disappear following ovulation. Surgical excision and mucosal resection can be accomplished in those cases where severe trauma or urine scald has complicated the condition.²²⁰ The urethra should be catheterized so that the surgeon does not resect through it. The surgical incised free edges are sutured together as the mucosa is resected usually with interrupted suture of 2-0 chrome gut. The area heals very quickly with little complication. In bitches with prolonged estrogen stimulation, such as hyperestrogenism from a granulosa cell tumor, the chronic prolapsed floor of the vagina may become organized with fibrous tissue and remain a large organized fibrous prolapsed mass that has to be removed surgically.

The most common genital tract abnormality of the queen is **uterus unicornis and segmental aplasia of portions of the reproductive tract**. (See Figures 153–155) One horn and possibly the ipsilateral ovary may be missing, or blind segments of the uterus are present that become more fluid filled with each estrous cycle.^{121,239} Stenotic or fibrous adhesions or complete-closure and scarring of the cervix in the queen is occasionally diagnosed as a cause of infertility. This usually results when a young nulliparous queen delivers one or two kittens and tears or traumatizes the cervix. Diagnosis is made following a history of infertility and examination of the cervix in a well-restrained or tranquilized queen with a small otoscope cone and light. The prognosis is poor for further breeding.

Neoplasia

Neoplasms of the genital tract are more common in the bitch than the queen, but increase in prevalence with

age in both. In the study by Andersen and Simpson of the aging Beagle bitches, hyperplasia of epithelial tubules, the so-called subsurface epithelial structures (SES) leads to adenomas, sometimes filling the cortex of the ovary with multiple microadenomas consisting of a complex of simple tubules.⁶ They also can be cystic or papillary. (See Figure 157) This can lead to **papillary cystadenocarcinoma** which can vary in size and can grow through the bursa and beyond the ovary. Surrounding tissue implanted by contact and metastasis via the lymphatics is common resulting in peritoneal ascites. Histologically, these neoplasms contain elaborate branching tubules with variable amounts of vascular connective tissue and cystic formation. In one Beagle bitch, a unilateral tubular adenocarcinoma caused death of this intact bitch at 14.3 years of age. The dog had estrous cycles until 12 years of age, followed by anestrus. At 12.2 years of age, ascites was detected and at death the peritoneal cavity contained 1600 ml of fluid.⁶ These tumors are usually bilateral instead of unilateral as reported in this case. The aging Beagle study listed ovarian adenocarcinoma of tubular origin in 9 of 59 (16%) control Beagles, with an average age of 13.5 years (11.0 to 16.6 years). Among all of the 216 Beagles examined, 42 carcinoma of tubular origin were found and 31 (74%) were composed of papillary and cystic structures. They found that most of them infiltrated or metastasized to other organs or structures in the abdominal cavity causing ascites at terminal illness.⁶

In this latter study, granulosa cell cords were most frequently seen in the corticomedullary junction and hyperplasia of these cords led to benign and malignant neoplasia. Benign granulosa cell tumors usually consist of solid groups of cords with dense cellularity. Granulosa cell carcinomas are composed of variable-sized anaplastic cell cords scattered throughout a highly vascular matrix of loose connective tissue. These tumors can have cells with high mitotic figures and can be quite invasive with spread to adjacent or distant organs. In the above study, 3 of the 59 aged control Beagles had **granulosa cell tumors**, which were malignant. Among 157 irradiated Beagles, 14 granulosa cell tumors were found, 5 of which were malignant. In this study, granulosa cell tumors comprised about one-fourth of the ovarian neoplasms.⁶

The World Health Organization classifies the ovarian tumors of domestic animals as follows; epithelial tumors as papillary adenoma and adenocarcinoma, cystadenoma and undifferentiated carcinoma; germ cell tumors as dysgerminoma and teratoma; sex cord-stromal tumors as granulosa cell tumors, thecoma and luteoma. In their report, epithelial and granulosa cell tumors occur with equal

frequency in the bitch, whereas granulosa cell tumors are more common in the queen.¹⁹² In their study, the canine papillary adenoma and adenocarcinoma share similar features with their counterpart in women with the same histological appearance, frequent bilateral occurrence with peritoneal implantations, ascites and metastasis. Papillary tumors in the bitch have been induced by prolonged administration of diethylstilbesterol.¹³³ The tumors were fairly small, the largest being 7 × 6 × 4 cm. The ovaries were largely replaced by shaggy spongy masses of proliferative tumor tissue that grew through the bursal sac. Peritoneal implants occurred in 5 of the 6 cases and lung metastasis occurred in 2 cases.¹³³ Six papillary cystadenocarcinomas in bitches 6 to 15 years of age were described with marked ascites in 2 and bilateral involvement in 3 cases.¹⁷⁴ Cystic endometrial hyperplasia with a blood-tinged vaginal discharge and irregular cycles was also described. This may not be directly due to the influence of the ovarian neoplasia, but probably more likely was an endometrial hyperplastic degenerative change with age.¹⁵⁴

Sex cord-stromal tumors are also known as gonadostromal or sex cord mesenchymal tumors. Sex cord tumors are of the granulosa cell tumor series and may have luteal, Sertoli, thecal or granulosa cell types and patterns or can have all cell types and patterns co-existing in the same tumor. **Granulosa cell tumors** are able to produce steroid hormones, estrogens and progesterone, that can result in either nymphomania or virilizing effects. Approximately 20 percent of the granulosa cell tumors in dogs are malignant. Luteomas, thecomas and granulosa cell tumors with Sertoli patterns are usually benign.¹⁹² Several case reports of granulosa cell tumors in dogs are in the literature. A 14-month-old female Golden Retriever was reported to have a malignant granulosa cell tumor with widespread metastases to the omentum, mesentery, diaphragm, liver, serosal surface of the urinary bladder and all regional lymph nodes.⁵⁸ A metastatic stromal ovarian tumor with metastasis to the liver, spleen, lung, and kidneys was diagnosed in a 7-year-old Greyhound bitch.²²² Another malignant granulosa cell tumor of the Sertoli cell type with metastasis to the kidney, liver, and uterus was reported in a 6-year-old Airedale bitch.⁵ An 8 × 10 cm thecoma was removed from a 10-year-old Toy Poodle bitch with uneventful recovery. No metastasis was observed at surgery.⁹²

The granulosa cell tumors are usually seen unilaterally, often presenting as a large, lobulated, firm mass with a yellow-white cut surface, maybe solid, but often containing cysts, hemorrhage and/or necrosis.¹⁹² The distinct histological characteristic of the granulosa cell

tumor is the formation of Cal-Exner bodies or rosette formations of cells around an amorphous or proteinaceous central cavity. The largest granulosa cell tumor in a series studied was $11 \times 9 \times 5$ cms. and weighed 213 grams.¹⁷⁴ Most bitches affected with this tumor had a cystic endometrial hyperplasia, endometritis, pyometritis complex and showed signs of hyperestrogenism. The author has observed a case of hyperestrogenism in a 5-year-old Springer Spaniel bitch with attraction of males, a moderate persistent prolapse of the vaginal floor through the vulva and a constantly cornified estrous vaginal epithelium. Ovariohysterectomy revealed a unilateral granulosa cell tumor. The bitch recovered uneventfully. A 10-year-old female dog with endocrine abnormalities and abdominal distention responded to removal of a granulosa cell tumor and a regimen of immunotherapeutics using a mixed bacterial toxin even though multiple metastasis were present. The dog was normal 2 years later.¹¹⁷ Case reports of an 11.5-year-old West Highland White Terrier and a 4-year-old Afghan hound with abnormal prolonged estrous activity were diagnosed as granulosa cell tumors producing estrogen and progesterone. The Afghan hound also showed acute hyperestrogenism toxicity with myeloid depression, thrombocytopenia and hemorrhagic diathesis from endogenous estrogen production. Both returned to normal following ovariohysterectomy.¹⁷³

Cystadenomas, found in bitches and queens appear to originate from the rete ovarii. They are usually multiple, thin-walled cysts containing a clear watery fluid and may replace with time the true ovarian tissue.

Germ cell tumors include **dysgerminomas** and **teratomas**. Dysgerminomas are seen in both bitches and queens and are malignant in 10 to 20 percent of the cases. These are analogous to the seminoma in the testes of the male and consists of a uniform population of large round or polygonal cells, with frequent mitotic figures and giant cells. It is a highly cellular tumor, with little connective tissue. It grows quickly and necrotic and hemorrhagic areas are frequently present.¹⁹²

Teratomas are rare tumors that contain a mixture of normal and neoplastic tissues from two or three germ layers. They may be solid or cystic and contain hair, skin, cartilage, bone, teeth or muscle. The left ovary of a 5-year-old virgin Alsatian bitch contained a large teratoma characterized by large cyst lined with stratified squamous epithelium, dermoid cyst, cartilage, fat, collagen bundles and smooth muscle.⁵⁹ The dermoid cyst is a special form of cystic teratoma with one or more cystic cavities lined by epidermis and epidermal appendages that may produce sebum, sweat, and hair which accumulates in the cystic spaces. The author has diagnosed

a unilateral dermoid cyst as an incidental finding in a routine ovariohysterectomy in a 2-year-old St. Bernard bitch. A malignant ovarian teratoma was diagnosed in a 3-year-old St. Bernard bitch. The left ovary contained a large mineralized mass, 26 cm in diameter, easily discernible on radiology and contained areas of skin, adrenal glands, hair follicles, dermoid cyst, nervous tissue, cartilage, bone, and glandular epithelium and areas of liposarcoma. Peritoneal metastases were composed of tissue resembling liposarcoma.⁷⁰

Metastatic tumors to the ovary of the bitch include pancreatic adenocarcinoma, mammary adenocarcinoma, lymphosarcoma, transmissible venereal tumor and reticulum cell sarcoma.¹⁷ Metastasis to the ovary frequently occurs in the developing corpora lutea if they are present. Lipomas and leiomyomas, fibroleiomyomas (fibroids) can be found in the bursa of the canine ovary.^{176,177}

In a California epidemiologic study of canine mammary and genital neoplasia, ovarian tumors occurred at an incidence rate per 100,000 of 4.6 with 1.9 malignant and 2.7 benign; 2.3 in the uterus, 0.5 malignant and 2.7 benign; 13.1 in external genitalia, 1.0 malignant and 12.1 benign; 319.3 in mammary glands, 92.2 malignant and 227.1 benign. In this study, most ovarian tumors were adeno-types with 33 percent being malignant. Of 44 ovarian tumors, 3 were dysgerminomas. About 75 percent of the uterine tumors were benign leiomyomas. **Vaginal tumors** were mainly either leiomyomas or fibromas. Vaginal tumors were approximately 12 times greater in intact versus neutered bitches.²²⁷

Tumors of the oviduct are considered to be rare or absent in the dog and cat.⁶ Only one irradiated Beagle had a uterine adenocarcinoma in the study of aging Beagles.⁶ Forty uterine adenomas were studied but they were benign and characterized by vascular connective tissue, scattered uterine glands and cystic cavities. Grossly, these adenomas protruded into the uterine lumen as a pink mass and were either spongy or firm. Two leiomyomas were reported in the wall of the uterus among the 216 aging Beagles. **Tumors of the uterus** in the bitch are rare, but include adenocarcinoma, fibroma, fibrosarcoma, leiomyoma, leiomyosarcoma, lymphosarcoma, and lipomas in the broad ligament.¹⁹² A uterine adenocarcinoma with metastasis to the myocardium was reported in a 7-year-old Beagle-Terrier cross.²⁴⁹

Leiomyomas and fibroleiomyomas are most frequently found in the vagina and vulva.^{38,66,67,69,175,176,177} Other tumors, lipomas, fibromas, neurofibromas, fibrosarcomas, transmissible venereal tumor (TVT), adenomas, and lymphosarcomas can also be found as vaginal and vulvar tumors.^{17,175} A vulvar leiomyosarcoma with metastasis to the spinal cord, lung, and external iliac

lymph node was reported in a 13-year-old Standard Poodle.¹¹⁹ Any of the skin tumors; squamous cell carcinoma, melanoma, histiocytoma, mast cell tumors, etc. can be seen on the vulva since embryologically it is of cutaneous origin.

Rare cases of chorioepithelioma of the placenta of the bitch were reported by early workers, but recent studies of the post-partum period in the bitch reveal longterm subinvolution of placental sites that would fit the description given by the early workers of chorioepithelioma.^{3,186,215}

Granulosa cell tumors in the queen are seen more frequently than papillary cystadenocarcinoma. More than half of the granulosa cell tumors in the queen are malignant and metastasize.¹⁹² A sex cord stromal tumor, androblastoma with Sertoli-Leydig cell pattern, or a granulosa cell tumor, was reported in a 6-year-old queen. The right ovary measured $7.5 \times 5.4 \times 3.6$ cm and was cystic in areas. The left ovary was inactive. The uterus had adenomatous hyperplasia indicating an estrogenic effect, although none was clinically recorded.¹²⁵ Prolonged estrus and alopecia has been attributed to granulosa cell tumors in cats.²³⁹ The right ovary of a 15-year-old thin, depressed female Persian had a large lobulated mass which contained granulosa cells in solid areas and lining cystic spaces. Metastases were present in the pelvic areas, dorsal abdominal wall, liver, lungs and right kidney. The cat was lethargic, anorexic with pale mucus membranes. A hemogram indicted hypochromic anemia with moderate erythropoiesis. These signs and findings indicate a hyperestrogenic state prior to euthanasia.⁴ An extra-ovarian granulosa cell tumor was diagnosed in a 5-year-old Siamese queen exhibiting estrus for 3–4 months together with weight loss. A $4 \times 3 \times 3$ cm mass on the distal left uterine horn, not connected to the ovary, was diagnosed as a primary granulosa cell tumor. Response with weight gain following ovariohysterectomy but later a relapse with metastases were found in the liver, kidney and spleen.¹⁰ Cystadenomas are quite common in the queen's ovary. Dysgerminomas accounted for 15 percent of feline ovarian tumors in one study.¹⁷ These can be malignant. Both malignant and benign teratomas in the ovary of the queen have been reported.²³⁹ Uterine adenocarcinoma and lymphosarcoma have been reported as metastases to the queen's ovary. Carcinomas, adenocarcinomas, adenomas, leiomyomas, fibroleiomyomas, lymphosarcoma have all been described in the uterus of the cat.^{17,182,226,239} A vaginal leiomyoma was reported to cause constipation in a cat.²⁵⁴

Canine transmissible venereal tumor (TVT) has been well-described by a number of workers.^{17,24,25,27,46,150,175,178,250} It is known by a variety of names;

Sticker tumor, infectious transmissible venereal tumor, transmissible sarcoma, transmissible lymphosarcoma or histiocytoma. It is easily transmitted by transplantation of cells by contact during coition, or by licking of the genitalia or extragenital tumor masses.¹⁹

In the United States, the incidence was formerly high around the large city areas such as New York City and Chicago. This miraculously has disappeared, probably because of better dog control programs and immune status of the population. More recently, areas of southern United States and the Caribbean Islands have higher prevalence.

This tumor can implant in any epithelial tissue. On a mucosal surface, the tumor appears as a glistening, nodular, cauliflower-like elevation that becomes larger and in many cases reseeds itself in the surrounding tissue. Although usually the genitalia are affected, it may also occur on the face, shoulders and other locations and may metastasize to lymph nodes and other organs including the spleen, liver, lung, tonsils, nasal cavity, brain and eye.¹⁷ Occasionally extragenital tumors are found with no primary genital tumors; although initial infection may have been the genitalia with regression by the time of clinical diagnosis.²⁵⁰ In advanced cases, a bloody, purulent fetid discharge usually is present from the vagina of the affected bitch. The tumor may protrude through the vulva of the bitch or involve the vulva itself. Large cauliflower-like masses may be seen on the prepuce and penis of the male dog. Occasionally the tumor can be pedunculated, nodular or papillary. They are often ulcerated and inflamed on the surface.

Histologically, the tumor is very cellular, consisting of large round cells which bear resemblance to lymphoid cells, histiocytic, or mast cell tumors, but the cells are usually larger.^{17,150} Mitotic figures are quite numerous even though the infiltrative and metastatic characteristics are low.¹⁵⁰ The cells of the venereal tumor usually contain only 59 chromosomes (58 to 60), 17 of them metacentric and 42 acrocentric.^{1,150} Normal cells of the dog at metaphase contain 76 autosomal chromosomes, all of them acrocentric. The sex pair are metacentric, the X is largest of the complement and the Y near the smallest in size.

C-type virus particles have been detected in TVT by electron microscopy, but attempts to transmit with cell-free filtrates have failed.²²⁴ Older dogs are susceptible, while young dogs seem refractory to experimental infection. Tumors grow to maximum size in 5 to 7 weeks and usually spontaneously regress in about 6 months.^{186,208} Treatment is often not necessary because of regression. Recovered dogs remain immune for long periods.¹⁸¹ Persistence and recurrence following surgery is due to a de-

iciency in cell-mediated immunity.^{39,250} This has been measured by a mixed lymphocyte culture test in which those dogs with tumor regression had a high lymphocyte blastogenic response to TVT cells compared to those that did not regress or had persistence with metastases.³⁹ Surgical removal is often curative. Persistent local lesions can be treated with X-radiation therapy with either single or divided courses totalling 2000–2400 rads.^{17,250} If metastasis occurs, chemotherapy with a combination regimen consisting of vincristine, cyclophosphamide, and methotrexate is highly effective.³⁹ Vincristine alone appears to be comparable to the above combination chemotherapeutically, with less side effects and easier management and therapy.⁴⁷

Mammary tumors in the bitch and queen are common compared to other domestic animals. In the bitch, tumors of the mammary gland are second in frequency only to tumors of the skin.^{150,175} An epidemiological study of canine mammary gland neoplasia in California revealed several interesting facts.²²⁷ Mammary gland tumors are seen in approximately one male case to every 100 female in the cat, and two male cases to every 100 female in the dog. Bitches spayed prior to any estrous cycle had 200 times less mammary cancer. Those spayed after one cycle had 12 times less risk and those spayed after maturity had no reduced risk. Regardless of age when spayed, overall reduction in risk is 5 to 7 times for most populations. Castrated males have the same rate as non-castrated.²²⁷ The lowest breed incidence was noted in Chihuahuas.^{79,227} If the incidence in Chihuahuas is equal to 1.00, then all other breeds are 1.75 to 4 times higher with the following rates reported: Pekingese, 1.15; Labrador Retriever, 1.74; Beagle, 1.75; Poodle (all sizes), 2.31; German Shepherd dog, 2.14; German Shorthaired Pointer, 2.60; Dachshund, 2.67; Cocker Spaniel, 4.03.²²⁷ Death rate the first year following malignant mammary tumor removal from bitches was 2.5 times the rate of bitches not having mammary cancer. The younger the dog, the longer the period before additional tumors or complications developed. Over 70 percent of dogs studied developed additional tumors.²²⁷ Within 42 months of the first diagnosis of mammary cancer, 50 percent of bitches 6 years or younger developed additional mammary cancer, whereas 75 percent of bitches 10 years and over developed such cancer.²²⁷ Others have reported similar findings.⁹¹ Spaying bitches after cancer development did not prolong life.²²⁷ In another epidemiological study, the incidence rate was 198.8 in 100,000 females. Tumor rate increased after 5 years of age.⁷⁹

Progesterone, endogenous secretion and exogenous therapy causes mammary gland hyperplasia and neoplasia in the bitch and queen. Researchers have found that

exogenous progestins, such as medroxyprogesterone (MPA), and cyproterone acetate (CPA) cause an increase in growth hormone (GH) or somatotrophin, and resulting mammary gland nodules and tumors. Prolactin (PRL) levels remain normal.^{64,101,102} Acromegaly following progesterone and GH increase was described earlier in this chapter. Both GH and PRL receptor sites are found in canine mammary gland tumors. It is believed that GH, stimulates growth of the gland and PRL mammary secretion.^{90,101,102} Antiprolactin drugs, such as the bromocriptine drugs, when administered to bitches with mammary gland nodules and tumors, or lactating bitches will cause a drastic reduction in size and secretion.^{138,183} The amount of progesterone influence of synthetic progesterone used for therapy will have different effects on the mammary gland. In one study of estrus control in 1011 bitches with progestin there was no increase in mammary tumor nodules among 331 given proligestone whereas 341 given medroxyprogesterone acetate (MPA) had increased nodule incidence over the 339 untreated controls (age groups 4–6 and 6–9 years of age, 19 and 39% for MPA and 5 and 13% for controls, respectively).²⁴⁵

In the California study, 67 percent of 4000 mammary tumors studied were mixed mammary types, whereas 32 percent were various adenomas and adenocarcinomas. Most mixed types were benign (6.5 to 1) while most adeno-types were malignant (2 to 1). The probability of malignancy increased with age. Spayed females over 3 years of age in the California study had a 5 to 10 percent increase of probability of having a malignancy over non-neutered females, therefore early neutering appears to spare benign development, but not malignancy.²²⁷

In another study of 226 canine mammary tumors, it was reported that both benign and malignant tumors increased in frequency from the anterior to posterior glands.⁹¹ Approximately 57 percent of all canine mammary gland tumors arise in the posterior glands.¹⁷⁵ In the previous study, where pseudopregnancy had been marked, there was a significantly increased chance of the tumor being malignant.⁹¹ Others have reported that the incidence of dogs with mammary tumors and normal dogs were similar with regard to normal and irregular estrous cycles, signs of pseudopregnancy, and pregnancy.^{37,94} Bloom noted that the mammary tumor was apt to grow rapidly during proestrus, estrus, and metestrus and tended to become smaller and firmer with retardation in growth during anestrus and after ovariectomy.^{24,25} In the study by Else and Hannant, 50 percent of malignant tumors were cured by surgery, metastases in 52 percent of cases caused death within one year.⁹¹ Metastases were most frequently to lungs (38%), liver (18%), regional lymph

nodes (12%), kidney (12.7%), spleen (10%) and peritoneal/pelvic fascia (5%). Similar incidences have been reported by other workers.¹⁸⁸ Mortality with well-circumscribed carcinomas was lower and median survival longer following surgery than those with tumors having irregular infiltrating borders; as 86 percent of the latter died in less than 6 months post surgical removal.⁹¹ In a study of 120 cases of mammary cancer, 117 females, 2 males and a 1 dog of undetermined sex, 8 were duct carcinomas, 38 lobular carcinomas from alveoli with 8 dogs having 2 primary tumors.¹⁸⁸ Another study revealed that 65 percent of mammary tumors were benign mixed tumors and 25 percent were adenocarcinomas with the remainder being a variety of benign or malignant tumors.¹⁸⁶ Cotchin described 424 mammary tumors from bitches: 249 were benign and 187 malignant. Metastases were present in only 41 bitches.⁶⁸

Classification of canine mammary gland tumors are varied. Most prefer to use a histological descriptive classification. Adenoma, either intraductal or acinar (secretory tissue), or fibroadenoma. Adenocarcinoma is either simple (epithelial only) or complex (both epithelial and myoepithelial) and consists of papillary (ductal), tubular (ductal), lobular (acinar), scirrhous, or adenocanthoma (portion containing squamous cell carcinoma within the adenomatous epithelium). There also are medullary or solid carcinomas, either simple or complex, or undifferentiated (anaplastic) carcinoma. Mammary adenocarcinoma in the dog comprises approximately one-half of all mammary gland tumors.¹⁷⁵ Mixed mammary gland tumors with both epithelial and mesenchymal tissue involvement, is usually the most common mammary tumors of the dog.^{150,175} This tumor contains glandular tissue, myoepithelium, myxomatous connective tissue, cartilage and bone. Mixed tumors are slow growing and less likely to metastasize. Sarcomas, usually less than 2%, are of the osteosarcoma, chondrosarcoma, fibrosarcoma or combined types. The so-called spindle cell carcinoma, rare in the dog, is of myoepithelial origin.¹⁵⁰ Frequently the malignant mammary gland carcinoma will ulcerate the overlying skin and exude a bloody discharge and a foul decaying flesh odor will be present.

Nodular hyperplasia of the mammary gland of the bitch is seen following progesterone therapy for estrous cycle control or during the luteal phase of the cycle.^{64,101,102} This is classified as cystic glandular hyperplasia and lobular hyperplasia or papillary cystic lobular hyperplasia and nodular papillary cystic myxodysplasia, respectively. Both types have ductal hyperplasia and sometimes myoepithelial cell formation, while the nodular or lobular form is the transitional form between hyperplasia and benign mixed tumors.^{150,175}

Ductal ectasia with accumulated milk secretion resulting in a periductal granulomatosis infiltration created by the accumulated secretion or stasis of milk in the gland called galactostasis will also cause a nodular mammary gland lesion.¹⁴⁷ These mammary gland dysplasias are fluctuant depending on stage of cycle. It is important when examining the bitch for breeding soundness or general physical examination to record the location, size and appearance of any mammary gland abnormality. The stage of estrous cycle and any exogenous progesterone therapy should also be recorded. On reexamination the mammary gland abnormalities can again be reevaluated and decisions made on treatment. The inguinal lymph nodes or fat pads in this area should not be confused with mammary gland nodules or tumors.

Mastitis does occur in the mammary gland of the bitch and queen and is caused by bacterial infection of the lactating gland postpartum or during pseudopregnancy. Enterobacterium, streptococci and staphylococci are commonly cultured. Broad spectrum antibiotics are given immediately, followed by specific antibiotics following culture and antibiotic sensitivity tests. Acute mastitis may progress to abscessation or gangrenous mastitis.^{104,147}

Feline mammary hypertrophy, also called juvenile fibroadenomatous hyperplasia is characterized by hyperplasia of both epithelial and stromal components. It can be seen in single glands or the entire chain.^{116,150,167} It is most frequently seen in young sexually intact females of 1 year of age or less following estrus and resulting during pseudopregnancy or during pregnancy and appears to be progesterone dependent. Progesterone receptors, but no estrogen receptors were found in hypertrophied mammary gland tissue.¹¹⁶ Spontaneous remission occurs and recurrence during following pregnancies or pseudopregnancy is usually not noted or with less involvement and appears to be a normal physiological hypertrophy.⁵⁶ Many of these affected queens have difficulty walking due to the extremely hypertrophied glands and are lethargic. Ulceration and excoriation of the skin over the enlarged glands is common. Secondary mastitis may occur. Antibiotic therapy is advocated when this happens as well as the use of warm water soaks.⁵⁶ Feline mammary hypertrophy has been shown to regress following ovariectomy. The clinical condition in young queen should not be misdiagnosed as a rapid growing mammary gland carcinoma with radical surgery of the complete mammary chain. Regression is usually noted in 2 to 3 weeks to 1 month after reaching maximal size. Treatment with bromocriptine drugs has not been reported, but the success in dogs with mammary gland hyperplasia and neoplasia in decreasing the size of the tumor masses should be studied in the queen. Mam-

mammary hypertrophy in older cats of both sexes following progesterone treatment with compounds such as megestrol acetate (**Ovaban**-Schering) for skin conditions or the control of tom cat behavior or urine spraying is progesterone-related. Removal of progestin therapy results in alleviating the nodular hypertrophy.¹¹⁶

Mammary tumor development in the cat comprises between 6 and 11 percent of all feline tumors. This incidence is much lower than that of the dog. Feline mammary tumors tend to occur at an older age than in dogs with an average of 11.5 years given by Cotchin.^{67,69} Mammary tumors in the cat arise more frequently in the anterior glands. The neoplasms are nearly always malignant, fast growing and between 75 and 86 percent being simple adenocarcinomas mostly of the papillary type, although the solid type is found. Recurrence following surgery is common. The most common sites of metastases are the regional lymph nodes and lung, but they can be found in the liver, adrenal, kidney, spleen and myocardium. A study involving 132 cats, including 2 males with mammary neoplasia revealed a ratio of 9:1, malignant to benign tumors.¹¹⁸ Adenocarcinomas were the predominant type.^{118,175,186} The Siamese breed had twice the risk of developing mammary carcinoma with an increased prevalence at a younger age, 7 to 9 years compared to the peak age incidence in other breeds at 10 to 14 years of age.¹¹⁸

Non-metastatic ovarian and uterine tumors can successfully be removed by ovariectomy. Mastectomy is indicated for mammary gland neoplasia. Regional lymph nodes and radiographs of the lung should be examined for metastases. Vaginal and vulvar tumors are frequently benign and pedunculated and can be removed easily after ligating the pedicle. When the base of the tumor is broad, a dorsal episiotomy may be indicated in order to obtain adequate exposure of the vagina and tumor so that complete excision can be accomplished.

When **malignant reproductive tract or mammary gland tumors** have metastasized to other organs, the prognosis is grave. New methods of treatment including radiation therapy, chemotherapy, immunotherapy and antihormone therapy can increase life span or in some cases cure the animal.

A bilateral ovarian papillary cystadenocarcinoma in a 5-1/2-year-old Coonhound bitch with ascites and several peritoneal and visceral tumor nodules was reported and treated with chemotherapy consisting of a combination of cyclophosphamide (**Cytoxan**: Mead Johnson) and chlorambacil and nitrosurea (**Cee Nu**: Bristol) following ovariectomy and removal of 4L of peritoneal fluid.¹⁰³ Four months post-operative, hydrothorax due to

malignant pleural effusion was diagnosed. The thorax was drained and infused with bleomycin (**Blenoxcine**: Bristol) which was removed 24 hours later. Ten months after diagnosis, the dog appeared in excellent health.¹⁰³

Crow gave an excellent summary on the treatment of malignant neoplasms of the reproductive organs and mammary glands of the dog. Radiation therapy can be used either as a primary therapy or as an adjunct to surgery or cryosurgery. Superficial single tumors such as transmissible venereal tumor or squamous cell carcinoma can be treated with up to 4000 to 6000 rads of external beam irradiation administered in 500 rad fractions three times weekly. Cobalt therapy can be used for deeper lesions.⁷¹

Chemotherapy is most often used in treating disseminated malignancies seen in ovarian and mammary gland metastatic malignancies. Use of anticancer agents are dosed on basic surface area and monitored daily for the following: weekly examination including packed cell volume (PCV), total white blood count (WBC) and differential and platelet quantitation. Cytotoxic agents are discontinued if PCV is less than 25 percent, WBC less than 3000/ul, neutrophils less than 1000/ul, and platelets less than 50,000/ul. A list of commonly used chemotherapeutic drugs by Crow included: chlorambucil (**Leukeran**), cyclophosphamide (**Cytoxan**), cytosine arabinoside (**Cytosan**), 5-fluorouracil (**Fluorouracil**), **Methotrexate**, Prednisone, vinblastine (**Velban**), vincristine (**Oncovin**). The reader is referred to the article by Crow for further information on dosage and use.⁷¹

Increased levels of circulating immune complexes were demonstrated and reported in the sera of bitches with both benign and malignant mammary gland neoplasia by a group of workers using a modified Raji cell technique.¹⁷² Dogs with persistent increases of circulating immune complexes were found to be at greater risk of developing metastatic cancer post-mastectomy. Significant anti-tumor response was found following immunoadsorption with staphylococcus whole organisms and treatment with saline supernatant staphylococcus preparation, incubated with plasma from solid tumor bearing bitches. The workers felt that tumor regression following staphylococcus reaction with plasma may be related to the release of a non-protein A bacterial product.¹⁷² A 10-year-old bitch with endocrine abnormalities and abdominal distention caused by a granulosa cell tumor was reported to have tumor metastases on the liver and partial peritoneum.¹¹⁷ Following an ovariectomy and removal of fluid from the peritoneal cavity, the bitch was given 4 months of immunotherapy consisting of a mixed bacterial toxin (MBT). This treatment has been used to successfully treat malignant ovarian and uterine neoplasia.

sia in women.¹¹⁷ Radiography 5 months post-surgery and 1 month post-immunotherapy revealed no metastatic disease with an apparent cure lasting two or more years. The use of bacillus Calmette-Guerin (BCC) to cause regression of experimentally-induced transmissible venereal tumor in dogs has been reported.⁴⁷ Bromoergocryptine drugs are antiprolactin in activity and when administered to bitches with mammary gland neoplasia cause noticeable regression in the size of the gland which has been beneficial in surgical removal of the tumorous masses.^{138,183} Combinations of surgery with radiation therapy, chemotherapy, immunotherapy or antihormone therapy appear to be highly beneficial in increasing the life span or curing dogs of malignant metastatic reproductive tract and mammary gland neoplasia.

Specific Infections of the Genital Tract

Specific infections of the genital tract of the dog causing infertility are *Brucella canis*, canine herpes and transmissible venereal tumor (TVT) (discussed previously in this chapter under neoplasia). Tuberculosis of the uterus in the dog has been reported, but is rare.²⁵

Brucella canis was first reported in 1966 as causing abortion in Beagle bitches.^{54,55} It is known now to be an established disease of dogs, occurring in all breeds of dogs with worldwide distribution and manifesting many clinical syndromes as well as a nonclinical carrier state.^{30,35,122,189,196,207,242,243} Human infections have also been reported. A literature review of 18 human cases revealed that this disease was of public health significance but that man was relatively resistant to ***B. canis***. Signs included headache, fatigue, enlarged regional lymph nodes, without splenomegaly, and mild fever.⁵³ Infected individuals responded well to tetracycline therapy.

Dogs are the only known natural host, although experimentally foxes and cats are highly susceptible.⁵³ Canine infections can also be caused by ***Brucella abortus***, ***B. melitensis***, and ***B. suis***, following contact with infected material, but the disease is usually self-limiting and the organisms do not persist.^{49,50}

A case was reported of a clinically normal pregnant bitch shedding ***B. abortus*** in urine, vaginal secretions and following euthanasia, isolates were made from the brain, mammary gland, and all lymph nodes. The bitch had been exposed to a ***B. abortus*** seven-month-aborted bovine fetus, 5 weeks prior to sampling and 3 weeks before whelping clinically normal pups. The pups were negative for ***B. canis***.²¹

Several excellent reviews on canine brucellosis have been published by Carmichael and other workers.^{49,50,51,53,54,55,131,184,214} In the bitch, clinical signs in-

clude abortion after 13 days but most commonly between 45 and 55 days of gestation. Some pups may be expelled dead and others alive, if after 55 days of gestation. Early embryonic death which appears as a failure to conceive is infrequently associated with ***B. canis*** infection. In the male, epididymitis and orchitis followed by testicular atrophy are common. A draining fistulous track can occur between the epididymis and the scrotal skin.^{99,228} General lymphadenopathy with enlargement of all lymph nodes is common in the infected dog. ***Brucella canis*** is readily isolated for several weeks from the aborted pups, placentas, and vaginal discharges post abortion. In the male, ***B. canis*** is easily isolated from the draining scrotal fistulous track and from semen and prostatic fluid of the clinically-affected stud dogs with prolonged carrier states and intermittent recurring acute infections occurring in the prostate gland. Infertility with poor semen quality, pus in the ejaculate and agglutination of sperm are common clinical signs in the effected stud dog.⁹⁹ Prolonged bacteremia lasting more than 2 years is characteristic of this disease. After several months the bacteremia may be intermittent.⁵³ Experimentally infected dogs have remained blood culture positive for as long as 5-1/2 years.

The most common non-reproductive disorder associated with seropositive status for canine brucellosis is discospondylitis and osteomyelitis.¹³¹ This is similar to ***B. suis*** infections in swine. Joint involvement may occasionally be seen. ***Brucella canis*** was also reported from a uterine stump abscess in a spayed bitch.⁷⁶

Many infected carrier animals may appear clinically normal, even though they are bacteremic and may shed organisms in the semen or possibly intermittent vaginal secretions. Clinically normal appearing males may shed the bacteria in semen and infect susceptible bitches venereally at breeding. It appears that the male is most likely infected via the oral route. It requires a minimum of approximately 2 million ***B. canis*** organisms to establish infection by the oral route.⁵⁰ Organisms can be isolated from the urine and vaginal secretions of affected bitches, but usually in insufficient numbers to infect others, although experimental infection can occur via all mucosal membrane surfaces such as the eye, nose, mouth and vagina. Contaminated needles used to draw blood or as a transfusion may cause disease in susceptible dogs.⁵⁰

Diagnosis of ***B. canis*** in an individual dog or kennel depends on an adequate clinical history, serology and bacterial isolation. Isolation of the organism from blood, semen, aborted fetuses and placentas and vaginal secretions is the definitive diagnosis. A rapid slide agglutination test that produces a presumptive diagnosis if positive is available (Pitman-Moore, Inc.). This test is highly accurate for the negative status since false negatives have

not been observed. Thus all dogs examined for breeding soundness or infertility should routinely be tested for *B. canis* using the rapid slide test. Positive reactions should be tested further since cross-reactivity to other antigens, such as some of the mucoid strains of *Pseudomonas aeruginosa*, *Staphylococcus* spp. and *Moraxella*-like organisms occur. Other tests that are more sensitive include the standard tube agglutination test (TAT) and the 2-mercaptoethanol test (2-MET) TAT. Titers of 1/200 for TAT and 1/100 for 2-MET are considered diagnostic.⁵⁰ Titers of 1/100 or higher usually indicate specificity for *B. canis*, but the definitive test is to isolate the organism from whole blood using either a blood culture tube or EDTA or heparinized blood. Titers of 1/100 or higher usually will yield *B. canis* from blood cultures because these titers are usually the direct response of a constant bacteremia. A more sensitive test offered by a few diagnostic laboratories is the AGID test using a cell-wall antigen of either *B. canis* or *B. ovis*. Another AGID test utilizing a cytoplasmic protein antigen is offered by the Diagnostic Laboratory at the New York State College of Veterinary Medicine.²³⁴ Animals that are positive by rapid plate, both TAT and 2-MET test at 1/100 to 1/200 or higher, and are positive on both AGID tests are considered serological positive and would probably yield *B. canis* on blood culture. Cultures of *B. canis* from enlarged lymph nodes, bone marrow, vaginal discharge, semen or prostatic fluids are also excellent definitive diagnostic tests.²³⁴

Once diagnosed the prognosis for cure is poor and it is difficult, time consuming and costly to eliminate the organism from affected dogs. Gonadectomy with treatment usually will control the spread of this disease to others. Complete elimination of *B. canis* from breeding dogs is difficult and intermittent shedding is possible. Two regimes of treatment have been used most successfully: (1) Tetracycline hydrochloride is given orally (tid) for 3 weeks at 30 mg/lb of body weight. A second course is given following 3 to 4 weeks without treatment. Streptomycin (20 mg/lb, bid) with or without sulfadimethoxine (25 mg/lb, bid) is administered with the second treatment of tetracycline.^{53,139} (2) Minocycline hydrochloride can be given orally (tid) for 14 days at 25 mg/lb body weight. Intramuscular administration of streptomycin (10 mg/lb, bid) is given for the first 7 days simultaneously with minocycline. These dogs must remain isolated from others during and following this treatment until checked negative at 6–8 weeks by both serological and blood culture tests before leaving isolation. Re-checks should be done at 6-month intervals for the next few years.

No vaccine is available to control the disease. The best management is to follow a constant surveillance program

recommended by Carmichael: (1) test all females with a history of recent abortion or infertility; (2) test males with scrotal irritation, epididymitis, orchitis, prostatitis, or poor semen quality; (3) test any new dog prior to introduction into the kennel; (4) test dogs that have been boarded for prolonged periods or used in field trials; (5) test dogs as a portion of all pre-breeding or fertility examinations.^{50,194}

Canine herpesvirus (CHV) is a cause of fatal septicemia in newborn pups, usually in the first week of life, but can be the cause of fatalities up to 1 month of age.^{48,52,88} It also has been reported to cause a granular or papular vulvovaginitis and balanoposthitis in adult dogs, and abortion; stillborns, mummification and infertility in bitches.^{52,113,114,115,123} Canine herpesvirus is widely distributed throughout the world and has been reported in the United States, France, Scotland, England, Japan, Australia, New Zealand and Switzerland.^{88,194,225}

In newborn pups, the virus is transmitted mainly by contact between the susceptible pups and infective oral and/or vaginal secretions of the bitch. The virus may also be spread by kennel owners or contaminated objects from other infected dogs to susceptible pups. The incubation period is between 3 and 8 days following intranasal injection. Healthy vigorous pups are observed to become suddenly dull, cry continuously, stop suckling and die within a few hours. There is no fever, but a marked thrombocytopenia develops. Usually entire litters are involved. The disease is characterized as an acute, often lethal, generalized necrotizing and hemorrhagic infection of all organs. One characteristic lesion is the multifocal areas of kidney hemorrhage and necrosis leaving the kidney with a "speckled" appearance. There may be a fibrinonecrotic pneumonia, multifocal hepatic necrosis, enlarged spleen and hemorrhage in various other organs of the body. The differential diagnosis is made by finding histologic intranuclear Type A inclusion bodies in some of the cells in the periphery of kidney or liver necrotic foci. This disease must be differentiated from canine hepatitis, toxoplasmosis, canine distemper, and bacterial septicemia caused by such microorganisms as *Escherichia coli*, beta-hemolytic streptococci and canine mycoplasmas and ureaplasmas.¹⁴⁵ There is no treatment once puppies are showing clinical signs. Subsequent litters in that kennel should be placed in an incubator at 95° F and 50–60% relative humidity since the infective virus appears to be temperature sensitive. Despite persistent infection of dogs, bitches that had lost their pups because of herpesvirus have not been reported to have additional losses at subsequent whelpings. Pups with maternal antibody are infected by CHV but do not become clinically ill since the infection remains localized, usually in the nasal area. In older susceptible pups or

dogs, the virus usually localizes causing a mild rhinitis or external genital tract infection. These animals usually demonstrate neutralizing antibody and have persistent low antibody levels for at least 2 years.

The genital form of CHV is characterized by multiple lymphoid nodules interspersed with petechia and submucosal hemorrhage in the vagina or on the penis and prepuce. There may be a preputial and vaginal discharge. Concurrently, there may be a conjunctivitis. Virus can be isolated from the nasal cavity, conjunctival sac, pharynx, and genital openings. Clinical signs following experimental infection lasted approximately 3 to 7 days. Both the conjunctivitis and genital disease are self-limiting and regressed in 4 to 5 days.¹²³

A condition called "dog pox" by European workers was thought to be canine herpesvirus and affected mainly the penis of the dog causing vesicular and papular lesions, thus the term "dog pox." Other sites affected were the conjunctiva, lower bowel, rectal-anal region, colon, and the vestibule of the bitch. In the series of animals studied by these workers, spontaneous regression occurred, but in some, lesions persisted for long periods of time.¹⁵² Lymphofollicular hyperplasia was produced in all normal puppies following the inoculation of cellular suspensions from affected dogs. No cytopathic effect was seen in the cell cultures even after 6 passages.¹³⁵ A noncytopathic viral agent or possibly a mycoplasma agent may be involved.

Inapparent infections are common in dogs and periodic shedding of canine herpesvirus in nasal secretions, similar to herpes infection in man and other animals can occur. Viral recrudescence has been demonstrated for as long as 6 months after primary intranasal infection by using immunosuppressant agents such as a corticosteroid.⁵²

Canine herpesvirus has been reported by British workers to be associated with abortion, stillbirths and infertility. Hashimoto and co-workers reported on spontaneous intrauterine infections of pups with CHV and experimentally showed transplacental infection of pregnant dogs by the intravenous route from day 30 through late gestation, resulting in mummified fetuses, dead feti, abortion, premature pups, stillborns and neonatal deaths. Characteristic lesions of CHV were found in the placenta, liver, spleen, kidney and lung of pups with virus isolation and a positive fluorescent antibody test for viral antigen in tissues.^{113,114,115}

Dogs showing active vesicular and papular genital tract lesions should not be bred. Swabbing of these lesions for culture and use of viral transport media to submit the swabs to a reputable diagnostic laboratory can be used to make a diagnosis. The best treatment is sexual rest until lesions have healed, which usually occurs in 7 to

21 days. Once exposed, most dogs will have a persistent low neutralizing antibody titer for at least 2 years. Recrudescence is uncommon unless the animals are severely stressed. Bitches that have had pups with neonatal CHV or abortions associated with CHV should be valuable breeders since this syndrome does not usually recur.

Urogenital disease caused by mycoplasmas and ureaplasmas have been recognized for years in man and cattle. They have been the cause of infertility characterized by poor conception, abortion, post-parturient septicemias, weak and diseased newborn, female and male genital tract infections. Poor semen quality has been associated with these organisms in both human and cattle infertility cases and in both, venereal transmission is recognized.⁷⁸

A survey of the mycoplasma flora of the dog by Rosendal revealed 11 *Mycoplasma* spp: *Mycoplasma canis*, *M. spumans*, *M. maculosum*, *M. opalescens*, *M. edwardii*, *M. cynos*, *M. molare*, *M. feliminutum*, *M. gateae*, *M. arginini*, *M. bovigentialium*, and one unclassified mycoplasma strain (HRC 689); 4 serological groups of ureaplasmas as well as *Acholeplasma laidlawii*.²¹⁸ In this study, mycoplasmas were cultured from the nasopharyngeal cavity of 100% of both healthy and diseased dogs; from the colon and rectum of 13% of healthy and 70% of diseased dogs, and from the lungs of 0–7% of healthy and 90–100% of diseased dogs. Mycoplasmas were rarely isolated from parenchymatous organs of normal dogs, but the incidence increased with systemic disease. Increased numbers of isolates were made from the reproductive tract of dogs with fertility disorders. *Mycoplasma canis* was the most common isolate from the canine genital tract, followed by *M. cynos*. *Mycoplasma cynos* is also a common pathogen of the canine respiratory tract. Several of the above species of mycoplasma have been associated with canine pneumonia, vaginitis, balanoposthitis, infertility, urine tract inflammation, colitis and endocarditis.²¹⁸

In a survey of 108 healthy dogs, mycoplasmas were isolated from the prepuce of 37 males and the vagina of 21 bitches (T = 58). *Mycoplasma canis* was isolated from 8 males and 14 females, *M. cynos* from 5 and 4, *M. bovigentialium* related strains from 11 and 3; respectively. *Mycoplasma edwardii* (2), *M. molare* (1), *M. opalescens* (6), *M. gateae* (12) and an unidentified strain HRC 689 (2) were isolated only from the prepuce of the dog.⁴¹ *Mycoplasma felis* was also reported from the canine genital tract by Doig and coworkers.⁷⁷ Mycoplasmas tend to be species-specific but in the above report, both bovine and feline strains are reported. *M. bovigentialium* has been isolated from several other species, including man.

Experimental chronic orchitis and epididymitis in the

dog and endometritis in the bitch were induced using a strain of *M. canis* isolated from the vagina of a bitch with an abnormal estrous cycle.¹²⁸ Mycoplasmal agents have been isolated and reported from three spontaneous cases of unilateral epididymo-orchitis by the author.¹⁶³ Canadian workers have found an association between canine mycoplasmas/ureaplasmas and infertility in stud dogs and breeding bitches.⁷⁷ They found a significantly higher incidence of ureaplasma in the prepuce of infertile stud dogs than those that were fertile and a higher rate of recovery from bitches that were infertile with purulent vulvar discharge versus those that were clinically normal. In the Canadian study, ureaplasmas were always isolated in association with a concomittant mycoplasma infection in the female. Ureaplasma was isolated in pure culture from the prepuce of one infertile male, whereas all others were in association with mycoplasmas.

Clinical studies carried out by the author confirm the Canadian workers findings. Clinical histories reveal a syndrome of infertility characterized by poor conception, early embryonic death, embryo and/or fetal resorption, abortion, stillborn pups, weak newborns and neonatal death. The Diagnostic Laboratory at the New York State College of Veterinary Medicine has isolated mycoplasmas and/or ureaplasmas from all phases of this syndrome. This syndrome is most frequently recognized in breeding kennels where close intensive living conditions and environment provide an opportunity for large numbers of these organisms to develop and affect the bitch and stud dog. Frequently, the same conditions are seen with bacterial opportunistic infections such as the beta hemolytic *Streptococci* spp., *Hemophilus canis*, *Pseudomonas* spp., *Proteus* spp., *Escherichia coli* and other bacteria found on the mucosa of the genitalia of dogs. Frequently, bacteria and mycoplasma/ureaplasma infections are mixed and concomittant. Historically, mycoplasma and concomittant bacteria cause severe disease or mixed infections in such conditions as chronic respiratory disease (CRD) of chickens and kennel cough in dogs. Intensive labor saving husbandry used for large numbers of closely-housed cattle results in a build up of mycoplasma and ureaplasma in genital and nasopharyngeal populations and can cause infertility in cattle.

Dogs kept for house pets in small less intensive managed kennels are not likely to be affected. In some infected kennels, several bitches will be involved and fertility rates may drop drastically. Normal reproductively sound dogs can also harbor these agents. Affected dogs may show no overt urogenital tract infections or discharges, but embryos, fetuses, or newborn pups may become infected in-utero following breeding, during pregnancy or at the time of whelping from the mycoplasma/ureaplasma/bacterial vaginal flora. In some individual

dogs, mucopurulent vulvar or preputial discharges are associated with vaginitis, endometritis or balanoposthitis, prostatitis and epididymo-orchitis, respectively.

Mycoplasma/ureaplasma/bacterial infertility in the bitch and stud dog should be suspected when a history of infertility is reported and characterized by reduced conception, early embryonic or fetal death, abortions, stillborns, fading pups, neonatal death, and metritis. Individual dogs with mucopurulent urogenital tract discharges and upper tract infections are also suspect.

Diagnosis is made by a history of infertility and isolation of the organism. A deep vaginal swab for culture is taken from the affected bitch with a guarded culture swab or a preputial swab or a sample of semen or prostate fluid is submitted from affected stud dogs. Aborted pups, placentas, post-resorption discharge, stillborn and dead neonates should all be submitted for culture and histopathologic study. Culture swabs should be placed in Amies transport media without charcoal (Amies transport media, Difco Laboratories, Detroit, Mich.) and sent refrigerated, **not** frozen, to a laboratory capable of isolating these agents. Entire pups and placentas should be iced, **not** frozen and also submitted. Since mycoplasma and ureaplasma organisms are very fastidious and require special media and a different atmosphere to grow, laboratories should be consulted prior to submission to find out if they are equipped, trained and capable of isolating and identifying these agents.

Bitches that are in large kennels affected with this syndrome are difficult to treat since there appears to be little immunity developed in the urogenital tract and the nasopharyngeal area against the carrier state of these microorganisms. Therefore, the syndrome continues through repeated breeding periods if adequate numbers of these organisms are present. The best control measures in affected kennels is to change the husbandry and management by isolating the bitches and stud dogs with or without chemotherapy, into smaller less intensive groups. This disperses and dilutes the population and contact so that the microorganism numbers of the carrier state are reduced.

Treatment for mycoplasma and ureaplasma infections or carrier states consist of parenteral treatment of small isolated groups with chloramphenicol or tetracycline, the drugs of choice for these microorganisms. Treatment should be given for 10 to 14 days. These drugs are contraindicated in pregnant bitches. Chloramphenicol is reported to be safe in the latter half of pregnancy.⁷⁴ Erythromycin or ampicillin, although not as effective against these agents, are safe to be used during pregnancy. A mild 1% tamed iodine solution (**Betadine**) vaginal douche may be administered two or three times during the parenteral antibiotic therapy. Bacterial infections should be

treated with the antibiotic showing the best antimicrobial effects. Records of pregnancy rates, litter size, and weaned puppy numbers are then assessed post therapy. Periodic cultures of the deep vaginal cavity of bitches with aborted or stillborn pups should be carried out. Reinfection can take place following treatment. Isolation of these agents from healthy dogs with no clinical signs of infertility does not require treatment since these agents are frequently normal flora and only cause problems when the numbers increase causing infertility problems. Further research to establish pathogenicity of species and strains and the role these agents play in causing infertility is needed.

Fisher in his survey on mortality in neonatal pups and kittens showed that the highest mortality was in the first week of life. He believed that the "fading pup" syndrome is caused by both infectious and non-infectious causes, but that the two causes can occur concurrently. Hypothermia, a non-infectious cause, enhances the growth of canine herpes virus in newborn pups. Initial starvation leads to low-colostral antibody uptake and leaves the neonate unable to deal with facultative pathogens. These organisms can then invade or proliferate in the gut of the neonate elaborating toxins or endotoxins which can lead to cardiopulmonary failure or appear as a non-infectious cause of death.⁹⁶

Miscellaneous Infections of the Genital Tract

Escherichia coli was isolated from the vagina of a 5-1/2-week pregnant Airdale Terrier with genital tract hemorrhage. Two fetuses were aborted on day 41 of gestation. Antibiotic therapy consisting of parenteral ampicillin, resulted in cessation of the hemorrhage until day 61 when again, an abnormal vagina discharge was observed. Caesarian section revealed 3 dead and 2 live pups which died within 2 days. *Escherichia coli* was isolated from the uterine contents.¹⁷⁰

Group B streptococcal septicemia caused neonatal death in 2 litters of Beagle pups in a breeding colony. The B streptococcal organisms were isolated from the vaginal secretion of both bitches following parturition. One bitch also had a postpartum septicemia. All pups appeared healthy at birth, but within 1 day, pups began to die. This appeared to be an ascending vaginal infection, similar to that reported for *E. coli*.¹⁵⁸

Microorganisms can also infect the uterus and puppies as a septicemia. *Campylobacter jejuni* and an unidentified *Campylobacter* sp. were isolated from aborted pups from 2 bitches. One bitch, a 1.5-year-old Wheaton Terrier, aborted pups on the 45th day of gestation following exposure to 2 children with an undiagnosed gastrointes-

tinal illness approximately 2 weeks previously. *Campylobacter jejuni* was isolated from the placenta, stomach contents of the pups and vaginal swabs from the bitch. The bitch showed no gastrointestinal disorder. This syndrome would be similar to that seen with *Campylobacter fetus* var *intestinalis* causing abortion in ewes and cattle. The other cases consisted of a kennel with adult dogs showing repeated episodes of diarrhea and vomiting followed by weak and dead pups at birth. Aborted pups showed histologic pneumonic lesions suggestive of bacterial or viral infections. Later, premature pups from another bitch were sacrificed and a *Campylobacter* sp. was isolated from their tissues.⁴² Another septicemia probably following oral ingestion of a microorganism resulting in abortion of pups was reported from 2 Boxer bitches. *Salmonella panama* was isolated from their aborted pups. During pregnancy both bitches were regularly fed cooked offal from a slaughter house and one of the bitches was fed uncooked tripe.²¹⁰ *Dirofilaria immitis* microfilaria were reported in newborn puppies and amniotic fluid of an infected bitch demonstrating that transplacental transmission of the microfilaria does take place in some bitches.²⁴⁴

Many bacteria have been isolated from the urogenital tract of the dog as reported in a recent literature survey by Jarvinen.¹³⁶ *Escherichia coli* was most frequently isolated from the urogenital tract which included the vagina and urethra of both normal and infected dogs.^{124,136} Other frequently isolated bacteria included *Streptococcal* sp., *Staphylococcus aureus*, *Proteus* sp., *Pseudomonas* sp., *Enterobacter* sp. and *Pasturella* sp.^{136,171,202} *Micrococcus* sp., *Corynebacterium* sp., *Bacillus* sp., *Staphylococcus epidermidis* and other unclassified bacteria were reported found in the vagina, urethra and infected urine. *Neisseria* sp., *Moraxella* sp., *Flavobacter* sp., *Hemophilus* sp., and *Clostridium* sp., as well as other anaerobic bacteria were reported found only in the vagina. *Klebsiella* sp., *Bordetella* sp., *Mimia* sp., *Alcaligenes* sp., and yeasts were found only in infected urine. *Nocardia* sp. was only isolated from the infected uterus.¹³⁶ Uterine culture results suggest that bitches do not normally harbor aerobic bacteria in the uterus.¹⁹⁹ Exudates from bitches with vaginitis contain the same bacteria as the normal vagina, but in greater numbers.¹²⁴ Vaginal swabs from 297 bitches with genital disorders yielded mixed cultures with *Streptococcus* sp., *E. coli*, *Staphylococcus* sp. and *Proteus* sp. the most frequent isolates.¹⁹⁸ Coagulase-positive *Staphylococcus* sp. were isolated more frequently from prepuberal bitches than from postpuberal bitches.¹⁹⁹

Another study revealed that aerobic and anaerobic mi-

croflora were identified and quantitated in 82 vaginal and 78 uterine samples obtained from mature bitches at different stages of the estrous cycle.¹³ The common organism isolated from vaginas were **Bacteroidaceae**, **Streptococci**, **Pasteurella** spp and **mycoplasmas**, **Staphylococci** and **mycoplasmas** were frequently isolated from uterine contents even though no histopathologic lesions were present in most uteri.

Anaerobic organisms were always recovered in mixed cultures, most frequently with **Proteus** sp.²⁰² In a study of 22 breeding kennels, 9 normal, 13 affected with "fading puppy" complex, **Cl. perfringens** was more frequently isolated from affected bitches (18/22) than from normal bitches (10/53).²⁸ This study indicated that **Cl. perfringens** can appear in the feces of apparently normal puppies 24 to 28 hours after birth and that possibly factors such as incorrect milk supplementation, hypothermia and prophylactic antibiotic therapy will affect the natural balance of intestinal flora and permit the microorganisms to gain pathogenic significance as it has been demonstrated in other neonates, such as lambs, calves and piglets.²⁸

Vaginitis should be suspected when abnormal vulvar discharges are present. Vaginitis can occur as a single entity or be part of an upper tract infection involving the cervix and uterus or the urinary tract. A thorough history and physical examination, utilizing a vaginoscope, vaginal cytology and culture, abdominal palpation and a complete blood count will help differentiate the extent of the disorder. Vaginitis can be secondary to foreign bodies and vaginal tumors. Vaginitis should not be confused with normal vulvar discharges of proestrus-estrous hemorrhage, normal lochia of the postpartum period or subinvolution of placental sites. History and vaginal cytology are important in differentiating these conditions. Non-infectious problems, such as vaginal tumors, clitoral hypertrophy and vulvar or vaginal congenital or acquired anatomical abnormalities must be considered in differentiating the cause. Occasionally vaginitis in the spayed bitch may be secondary to a fistula from an infected uterine stump or a stump abscess or granuloma. Vaginoscopic examination, abdominal palpations and radiography may be needed to confirm the etiology. The author has seen one case of tetanus following a routine ovariohysterectomy performed with surgical instruments used for both large and small animal surgery that were routinely cold sterilized in disinfectants. **Clostridium tetani** organisms were present in the uterine and ovarian stumps at necropsy.

A vaginal swab must be obtained for culture from the anterior vagina using a sterile guarded swab or a sterile otoscope head and a smaller sterile unguarded swab as

described in the section under mycoplasma/ureaplasma/bacterial infertility. The anterior vagina of larger dogs can also be cultured by placing a glide (**Playtex Gentle Glide**, Playtex, Inc., Dover, Delaware) in the posterior vagina and then pass a guarded culture instrument through the glide into the cranial vagina as described by Olson.^{198,199,201} Transport media for aerobic, anaerobic, mycoplasma/ureaplasma and viral microorganisms are commercially available from several scientific companies.

The entire vagina should be evaluated for inflammation or other abnormalities such as tumors, foreign bodies, anatomical problems, by a sterile fiberoptic vaginoscope or modified infant human proctoscope or otoscope in the case of the small dog or cat. Smears for cytology should be examined for the type and extent of inflammation and presence of microorganisms. Large numbers of toxic and degenerate polymorphonuclear leukocytes containing phagocytized bacteria are usually present in dogs with vaginitis. Non-toxic polymorphonuclear leukocytes are present in normal dogs in the early metestrus/diestrus period. Bacterial culture results should be interpreted as to their significance taking into account the number of organisms isolated, ranging from none or scant to moderate and many, pure or mixed culture, vaginal cytology and history of vulvar discharge and infertility, and the vaginoscopic exam findings indicating an active inflammation or no evidence of inflammation. Antibiotic sensitivities on isolated microorganism should be obtained and followed for the most successful therapy. Parenteral antibiotic therapy is discussed under the section on mycoplasma/ureaplasma/bacterial infertility. Parenteral therapy is most desirable because of its effect on other potentially affected sites, such as the nasopharyngeal and urinary tract. Antibiotics may be infused directly into the vagina or applied as vaginal suppositories with or without systemic antibiotic therapy. Mild antiseptic douches, such as a tepid 1% tamed iodine (**Betadine**) solution are useful in chronic vaginitis and are delivered as a high volume douche by passing a disposable plastic treatment pipette into the anterior vagina and lavaging the entire vaginal canal. In smaller dogs or cats a disposable bovine teat cannula or a tom cat or dog urethral catheter can be passed and by syringe the vagina can be lavaged. The author utilizes this lavage treatment regimen along with systemic antibiotics usually 2 or 3 times during a 10 to 14 day systemic treatment. Judicious use of estrogens such as oral 0.5 to 1.0 mg diethylstilbestrol tablets for 5 days or 0.25 mg of ECP administered intramuscular may be helpful in spayed bitches or prepuberal bitches with vaginitis.

Puppies can have vaginitis prior to puberty. Juvenile

vaginitis is not normal, and is usually difficult to cure, but usually subsides without treatment following the first estrus.^{198,199} Vulvar-vaginal anatomical abnormalities should be ruled out. If therapy is necessary, cultures prior to therapy should be studied, antibiotic sensitivities performed on significant isolated microorganism and these results used for the most effective treatment required.

Vulvitis may occur with or without vaginitis. The vulva is usually hyperemic and edematous. The bitch may be quite uneasy and lick the vulva after frequent urination. Difficult and frequent urination may be present. Vulvar-fold or perivulvar pyodermatitis is a common disease of obese dogs with immature, juvenile or inverted small atrophic vulvas. Many of these dogs have been spayed. Urine scald and urinary incontinence aggravates the problem. Some dogs may become febrile and septic when this condition becomes an acute deep ulcerative pyodermatitis. Culture of the vulva or perivulvar tissue may be obtained for specific microorganisms and tests for antibiotic sensitivity test result in the most successful therapy. Systemic antibiotics and anti-inflammatory drugs are frequently used when this condition becomes systemic. Otherwise, frequent cleaning and topical antibiotic, anti-inflammatory or chemotherapeutic ointment or powders are applied daily. Judicious estrogen therapy as described for vaginitis treatment may be used. The most successful method has been episiotomy, the surgical removal of excess perivulvar skin folds and the repair of the perineum with improved caudal positioning of the vulva.^{80,157}

Clitoritis and granular or lymphoid nodular hyperplasia of the vulva and/or clitoral fossa may cause a mucopurulent vulvar discharge, licking of the vulva and attraction of males. It may be seen in prepuberal, intact cycling or spayed bitches. This condition can be caused by any irritant, microorganisms, anatomical abnormalities, clitoral hyperplasia, especially noted following the use of androgen therapy, and in pseudo- or true hermaphrodites (see section on congenital defects). Treatment with mild antibiotic and/or anti-inflammatory ointments or mild cauterizing ointments and liquids are beneficial. Anatomical problems should be corrected surgically. Clitorectomy may be necessary with clitoral hyperplasia, especially with the presence of an os penis. Persistent or recurring vulvar or clitoral lymphoid nodular hyperplasia is best treated by sedating the bitch and scraping the granular or lymphoid nodules with a scalpel blade or sterile gauze pad until they hemorrhage or are removed. Following the control of hemorrhage, post-operative therapy consisting of 2 or 3 times a day application of an antibiotic and anti-inflammatory ointment (**Panalog**—Upjohn Company, Kalamazoo, Michigan) is

helpful. This will usually result in a temporary, if not a complete cure. If this condition recurs, repeated treatment and further examination to find the cause, especially if an anatomical abnormality is present, may be necessary. This condition can be very difficult to completely cure in some bitches.

Inflammation of the ovary and oviduct in the dog is rare. Abscess of a corpus luteum or pyosalpinx may occur secondary to a pyometra.^{24,25}

Cystic Hyperplasia, Endometritis, Metritis and Pyometra

Cystic hyperplasia, endometritis, metritis and pyometra, in the dog and cat are common and may be seen in intact bitches and queens of all ages, but is most frequently seen in animals over 3 years of age. **Pyometritis** in the bitch and queen can occur spontaneously, secondary to a systemic bacterial disease process, a postpartum metritis or following iatrogenic administration of long-acting progestational compounds to delay or suppress estrus, or following the administration of estrogens to mismated bitches or to treat juvenile or senile vaginitis, as a post-copulation or post-insemination infection, and as the final sequela of cystic endometrial hyperplasia-pyometria complex.^{7,165,233} This complex most commonly occurs in bitches starting at 3 to 4 years of age. The incidence increases with age and several non-pregnant cycles. This complex also affects intact queens and increases in incidence with age following repeated non-productive matings, pseudocopulation and spontaneous ovulation.

Canine pyometra is an acute or chronic polysystemic, metestrous disease of the mature dog.¹⁰⁶ In the bitch and queen, progesterone plays the major role in producing endometrial hyperplasia as this condition can be produced most promptly by the alternate administration of estrogen and progesterone. Exogenous estrogen alone can produce marked hyperplasia and endometritis followed by pyometritis in the bitch. Cystic endometrial hyperplasia may lead to mucometra or hydrometra and atrophy of the myometrium. An unusual case of uterine enlargement in a 12-year-old female Poodle with progressive abdominal enlargement and dyspnea was reported.⁹⁸ The cause of the uterine enlargement was cystic endometrial hyperplasia and adenomyosis. Another report of a 10-year-old female miniature Poodle with a pendulous abdomen for several months was diagnosed as hydrometra following surgical removal.¹⁴¹

Dow reported 4 subdivisions or gradations of the cystic hyperplasia-pyometra complex in the dog.^{81,82,83} **Type**

I was characterized by uncomplicated cystic hyperplasia of the endometrium with a mucoid discharge during metestrus. Twenty-three of the 100 bitches in the study were in this group. **Type II** was characterized by diffuse plasma cell infiltration of the endometrium superimposed on cystic hyperplasia. There were 17 of the 100 bitches in this group and in 14 animals *E. coli* was cultured from the uterus. A mucous discharge from the vagina persisted for several weeks in the metestrus/diestrus period and a mild leucocytosis was present with 12,000 to 15,000 W.B.C. per cmm. **Type III** was characterized by an acute endometritis, metritis or pyometra superimposed on cystic endometrial hyperplasia. The distention of the uterus was dependent on the patency of the cervix. Forty-nine of the 100 bitches were of this type. *E. coli* was cultured from 40 bitches, staphylococci from 6 and streptococci from 5 bitches. Most of these cases were presented 5 to 80 days with an average of 30 days after estrus. Illness of 4 to 10 days duration had been present with 32 dogs experiencing increased thirst, and 21 had vomited. Thirty-eight of the 49 bitches had a vulvar discharge; 40 had a distended abdomen and 8 had an elevated temperature. A leucocytosis with white cell counts of 19,000 to 145,000 per cmm, mainly neutrophils, was present. Counts over 50,000 per cmm were indicative of pyometra. **Type IV** was characterized by a chronic endometritis, often with squamous metaplasia of the endometrium. The chronic endometritis was either mild or severe with corresponding degrees of leucocytosis, abdominal distention and illness. These dogs were usually 10 to 13 years of age. There were 11 cases in this group.

It was significant that corpora lutea were present in the ovaries of 96 of the 100 bitches in the study. Ovarian cysts were present in 19 and granulosa cell tumors in 8. Most of the bitches had shown irregular estrous cycles. A history of previous attacks of postestrous endometritis, especially in **Type IV** cases, was common. Nearly all were nulliparous or had had litters 3 to 11 years previously. A few had histories of phantom or false pregnancies.

Dow also reported rather similar groups of cases in cats affected with the cystic hyperplasia-pyometra complex.⁸⁷ **Group I** consisted of 16 of the 100 unselected intact nulliparous female cats that had cystic glandular endometrial hyperplasia without any superimposed inflammatory changes. Most of these cats were over 3 years of age. Four of these cats exhibited hemorrhage from the vulva from which one cat died, and the others had a chronic discharge of blood and were severely anemic. This bleeding was due to torsion of endometrial polyps that ranged from 1 to 6 cm in length and were attached by narrow pedicles. **Group II** consisted of 39 cats, 3 to

11 years of age. Most were nulliparous and nearly half had been in estrus within 2 months. These queens had an acute endometritis and pyometra with an illness that had been present for 3 to 14 or more days. The inflammatory reaction was superimposed on a cystic hyperplasia of the endometrium. All cats in this group were dull, depressed and anorexic. Vomiting was a fairly common sign. The vulvar discharge was green, brownish or blood-stained in two-thirds of the cats; abdominal distension also was present in about 60 percent of the affected cats in this group. Total blood leucocyte counts ranged from 23,000 to 74,000 cells per cmm. Thirty-four of these 39 cats were treated successfully by ovariohysterectomy. Many uteri contained variable amounts, up to 2 liters, of pus; the pus was yellow-green in color unless bleeding had occurred into the uterus. Thirty-two of 37 cases were positive on culture for *E. coli* and six yielded streptococci. Corpora lutea were present in 33 of the 39 queens; a few follicles or follicular cysts were present in the remainder.

Group III consisted of 10 of the 100 cases. These cats had a subacute inflammatory reaction superimposed on cystic endometrial hyperplasia. Cats in this group were 4 to 11-years-old, and 7 were nulliparous. Illness was marked but of a longer duration, of 2 months or more, than Group II. Total white cell counts ranged from 21,000 to 32,000 per cmm. A chronic vulvar discharge was present. Most of these cats were thin. The uterine horns were slightly enlarged containing about 10 to 15 ml of greenish-grey mucopurulent exudate. *E. coli* was recovered from all uteri. Luteal tissue was present in 9 of the 10 cases. **Group IV** contained 22 queens with chronic endometritis and cystic endometrial hyperplasia. Their ages ranged from 5 to 14 years, and 14 of them were nulliparous. Fourteen of these cases had shown an intermittent vulvar discharge for 3 to 10 months; all 14 recovered after ovariohysterectomy. The remaining 8 cats were ill, some near collapse, with the history of a chronic low-grade endometritis with a discharge and an acute illness occurring within the last 7 to 10 days. In all of these 8 cases the abdomen had recently become greatly enlarged and anorexia was present; 4 of these cats had severe attacks of emesis. W.B.C. counts ranged from 24,000 to 64,000 per cmm. In these cases the cervix was patent and the uterus was only moderately enlarged. *E. coli* was isolated from 18 and hemolytic streptococci from 6 of these queens. Corpora lutea were present in 18 cats; 2 cases had normal follicles and 2 cases had follicular cysts. There was a degree of cervical fibrosis in all cases. In the distended uteri; all layers of the uterine wall were atrophied. Atrophy and squamous metaplasia of the endometrium were present in most cases.

In these 4 groups of cats over 75 percent were over 6 years of age. No cats under 3 years of age had cystic endometrial hyperplasia. The similarities between this complex in the bitch and queen are striking. There is also a similarity between these older affected bitches and queens and the "infection prone" older and often nulliparous mare. Over 77 percent of affected cats were nulliparous and had corpora lutea in their ovaries. Dow speculated on this high incidence of corpora lutea present in older nulliparous cats, a species that is considered to ovulate only after the stimulus of coitus. He indicated that possibly petting and stroking of the cat by the owner might be sufficient to induce ovulation. This disease in cats seldom appeared during the anestrus season of October through January. In the cat, as in the bitch, pyometra often becomes clinically evident in the metestrus/diestrus or pseudopregnant period. In breeding queens, early signs of cystic endometrial hyperplasia and a low grade endometritis were characterized by a succession of normal pregnancies, followed in order by stillbirths, a decreased number of fetuses in a litter, abortion at 42 to 52 days, and finally endometritis and sterility.

Dow showed experimentally that cystic hyperplasia-pyometra complex in the cat and dog were basically similar.^{84,87} In the latter species the cystic endometrial hyperplasia could be produced by cyclic treatment with estrogens and progesterone. The inflammatory reaction of endometritis and pyometra is progesterone-dependent. Progesterone greatly increases the susceptibility of the uterus to infection, maintains the functional closure of the cervix and causes a relaxation of the myometrium.^{175,176,177}

Further evidence of the hormonal basis for this syndrome is the numerous reports in the mid-sixties describing cystic glandular hyperplasia, mucometra, and pyometra in bitches injected with progestational compounds, such as medroxyprogesterone acetate (**Promone**—Upjohn) given intramuscularly or subcutaneously to prevent estrus. These long-lasting injections would effectively suppress estrus and ovulation for 6 to 24 months or more. Not all bitches or queens would develop endometritis and pyometra but a sufficiently large enough number, over 10 percent, were affected that these products were withdrawn from the market and presently are contraindicated, especially for a female that is expected to be bred at a later date.³⁶

In dogs severely affected with acute pyometritis, a high white blood cell count, septicemia, and a febrile reaction are common. The total white blood cell (WBC) count ranges from 20,000 to 100,000 +/cu mm. Higher counts are associated with the acute syndrome and a closed cervix or closed pyometra versus an open draining pyome-

tra with a vulvar discharge and a lower WBC count. Chronic cases or prolonged cases with toxemia result in bone marrow depression and anemia. The WBC may be lower than normal with frequently a shift to the left or increased band cells. Laboratory findings may include varying degrees of one or more of the following: regenerative neutrophilia, degenerative neutropenia, anemia, azotemia, hyposthenuria, hyperproteinemia, hypercholesterolemia, hypoalbuminemia, hyperbilirubinemia, and elevated BUN, alkaline phosphatase, LDH and PCV (dehydration).^{31,32,33,34,105,106,107,108} Polydipsia, and polyuria are frequent signs of pyometritis. Ascheim has shown that a membranous glomerulonephritis may be present and that the lesion by electron microscopic study is a membranoproliferative glomerulonephritis caused by immune-complexes.¹² Impaired renal tubule capacity to concentrate urine in dogs with pyometra is also common. This inability to concentrate urine is caused by endotoxemia.^{31,107} *Escherichia coli* and probably other bacteria probably play an important role as the cause of the antigen for the immune-complex disease and production of endotoxin in this kidney syndrome. Both of these kidney disorders are reversible following hysterectomy or successful medical treatment of pyometra. *Escherichia coli* strains isolated from urine specimens as well as from the infected uterus were identical.²²³ This study concluded that subclinical urinary tract infection is associated with pyometra and that the uterus will be infected at early metestrus, when receptors for *E. coli* are developed in the progesterone-primed endometrium and myometrium, thus enhancing the colonization of bacteria in the uterus.²²³ Adhesion studies have confirmed that urogenital isolates of *E. coli* have a specific trophism and receptors for binding to this tissue.¹³⁶

Pyometra is also associated with liver malfunction, usually as intrahepatic cholestasis sometimes followed by hepatocyte degeneration.²⁴ Endotoxin from *E. coli* may result in adrenal cortical necrosis and medullary hemorrhage and endotoxic-type lung damage in the terminal case.³⁴ Pyometra is unique in the magnitude of endotoxin effects with the uterus, kidneys, bone marrow, liver and probably other organs being affected and suffering disturbed function until the infected uterus is removed or successfully treated.³¹

The cytology of vaginal smears may be diagnostic in cases of pyometra with either an open or closed cervix. Most dogs in early metestrus/diestrus will have non-toxic normal polymorphonuclear leukocytes (neutrophils). By the 10th to 20th day postestrus, most neutrophils have disappeared and only small, non-cornified or larger epithelial cells containing a large round nucleus with some having highly vacuolated cytoplasm are present. Vaginal

cytology from dogs with pyometra is characterized by excessively large numbers or masses of toxic, degenerate neutrophils undergoing necrocytosis. The more toxic the environment, the more rapid the death of these cells characterized by karyolysis, karyorrhexis and pyknosis.^{18,106,201}

The presence of pyometra can be detected in most dogs with little difficulty, especially an open draining pyometra. Closed pyometra may be more difficult to diagnose. A pregnant bitch without a history of recent breeding may pose a problem since the enlarged gravid uterus is radiographically indistinguishable from a pyometra until skeletal structures of the fetuses are seen after about 43 to 45 days of pregnancy. Many pregnant bitches may be anorectic similar to those with an early pyometra. Ultrasonography is a preferred procedure to detect viable fetuses from approximately day 22 to 26 of pregnancy to term. Both closed pyometra and pregnancy develop following estrus. Prior to surgical removal, the uterus should always be carefully palpated to confirm the diagnosis of pyometra or pregnancy. A total white blood cell count is helpful. Pregnant bitches will also have a pregnancy anemia, but this is a hemodilution effect and not a true anemia. A moderate leucocytosis may be seen in later pregnancy as a result usually of increased eosinophils probably elicited by fetal-placental antigens and/or parasite larval antigens. Closed pyometra will usually have a severe leucocytosis with a shift to the left or a toxic leucopenia, but still with a shift to the left.¹⁶⁵

The clinical signs associated with pyometra and renal failure may be similar. Diseases associated with polyuria and polydipsia including diabetes mellitus, hyperadrenocorticism, and generalized hepatic diseases may simulate pyometra. All of these conditions may cause a pendulous abdomen and similar clinical signs and indeed may occur concomitantly with pyometra. Diagnosis can usually be made from clinical signs, laboratory tests, radiographs or ultrasonographs and microscopic examinations of vaginal smears. Urinalysis, hemograms and serum concentration of creatinine or BUN should be evaluated in the suspicious cases. Other appropriate diagnostic tests may be needed in the clinical and laboratory evaluation of the patient.^{106,165} Unusual cases of pyometra have been reported. Pyometra has been diagnosed in a male hermaphrodite with retained testes containing a Sertoli cell tumor and a uterus with pyometra.¹⁹¹

The early syndrome of cystic endometrial hyperplasia with or without superimposed endometritis may be associated with a blood-tinged discharge. Frequently there are no clinical signs. Infertility, small litter size, early embryonic death, abortions, and irregular estrous pe-

riods may be other indications of cystic endometrial hyperplasia. The lifetime reproductive history of this individual is important. The use of soluble radiopaque fluid to perform a hysterosalpingography and outline the cystic formations or the use of ultrasonography to possibly view the fluid-filled cysts are highly desirable. Hysterosalpingography should only be done on the non-infected uterus during estrus or anestrus when the cervix is open. If the uterus is infected, retrograde infection of the oviduct, ovaries and peritoneal cavity can take place. Palpation of an endometrial cyst 1 cm or more in diameter may be possible in some dogs and cats. Laparotomy or use of a laparoscope and biopsy of the uterus are also useful. Endometritis, and certainly metritis will be characterized by a vulvar discharge plus the signs mentioned earlier for cystic endometrial hyperplasia.

Cystic hyperplasia of the endometrium may involve all or part of both uterine horns or all or part of one horn.²⁵² Adenomyosis, or the presence of endometrial glands in the uterine muscle is common in some bitches. On the serosal surface these may have a gross appearance of a leiomyoma or fibroid until cut across and the "swiss cheese" appearance of the cystic glands in the muscle are noted. Pyometra following parturition or abortion in the bitch is seldom observed unless a dystocia handled with poor hygiene or a dead fetus and/or retained placenta causes a severe metritis which usually results in a very thin-walled friable and sometimes emphysematous uterus filled with a thin fetid serosanguinous exudate. Uterine rupture and parametritis are common sequelae because of the thin wall and acute nature of this condition. If a bitch is regularly pregnant, pyometra does not occur. Canine pyometra is usually seen with corpora lutea present in the ovaries and/or occasionally cystic follicles or lutea cyst. Several early workers felt that prolonged and/or high progesterone levels from retained corpora lutea or luteal cysts were the cause of pyometra. In a study by Chaffaux and Thiber, they found no evidence of an essential high or prolonged progesterone secretion in bitches with pyometra. Luteolysis occurred normally about 60 days postovulation and was not postponed by pyometritis. In some animals early luteolysis occurred.⁵⁷

Other uterine lesions noted in cystic hyperplasia and secondary endometritis are: edema, hemorrhage, diffuse leukocytic infiltration of the endometrium, fibrosis of the uterine wall, and occasionally ulceration, abscessation, necrosis, and thrombosis. The cystic endometritis tends to be latent or quiescent at all stages of the cycle except metestrus, at which stage most cases exacerbate under the influence of progesterone with clinical signs of varying degrees of severity. In pyometra there is a cystic

hyperplasia of the endometrial glands and severe leukocytic infiltration of the endometrium. The cystic glands may or may not be filled with exudate. Certain portions or most of one horn may be more severely affected than other portions of the same horn or the opposite horn. Necrosis of the endometrium may be present in advanced cases. The myometrium may show some evidence of fibrosis and invasion by endometrial glands or adenomyosis. If pyometra and stenosis or functional closure of the cervix results in distension of the uterus, all layers of the uterine wall are markedly stretched and atrophied.

Symptoms of the cystic endometrial hyperplasia-endometritis-pyometra syndrome in the dog and cat are as follows:

In cystic endometrial hyperplasia seen in intact animals over 3 years of age no clinical signs of illness are present, as no infection is present in the uterus. The vulva may be hypertrophied and swollen the first half or throughout the metestrous period. There may be an excessive discharge of mucus from the vulva that contains no bacteria, red blood cells and few or no leucocytes. Atresia or functional closure of the cervix may produce mucometra or hydrometra with one or usually both horns distended by a clear, watery or yellowish-grey, non-odorous fluid with a secondary distension of the abdomen in a few cases.

In cystic hyperplasia associated with endometritis and metritis, clinical signs and illness usually appear in the metestrous period, 10 to 90 days after estrus. Breeding may or may not have occurred. Some veterinarians report that affected bitches often have a history of breeding failures, irregular estrous cycles, pseudopregnancy, and are nulliparous. A study of affected bitches and 248 intact control bitches of the same age, average 7.7 years, found there was no correlation between estrous cycle irregularities, abnormal estrus, pregnancies, and cystic endometritis and pyometra.⁹⁵ Pseudopregnancy characterized by lactation, and abnormal signs exhibited by the bitch about 60 days postestrus was observed less frequently in dogs that developed an infected diseased uterus than in the control dogs. The injection of progestagens causing a prolonged progesterone-like effect on the genital tract and an artificial anestrus may cause this syndrome in young, one to two-year-old bitches.³⁶

Dogs and cats with secondary endometritis and metritis may or may show signs of illness with an elevated temperature and heart rate, anorexia, dullness, debility, and a rough, dull haircoat. The blood leucocyte levels are often somewhat elevated to 20,000 to 30,000 per cmm. Most of these animals will have a fetid mucopurulent discharge from the vulva that will persist for several weeks or more and must be differentiated from a discharge caused

by a vaginitis or cystitis. After a number of weeks, the signs spontaneously regress only to reappear following the next estrous period often in a more severe form. Chronic endometritis may be associated with stillbirths, abortion, embryonic deaths, small litters and infertility in dogs and especially cats.

In pyometra there is usually a nearly complete closure of the cervix preventing the escape of the mucopurulent, odorous exudate from the uterus with a distension of the uterine horns and definite to marked signs of illness, usually occurring during the metestrous period. The general condition and hair coat may be good or poor, depending upon the acuteness of the onset of the condition. Pyometra may develop rapidly within a week or may take several months. The body temperature in acute cases may be elevated, in chronic cases normal, or in severe toxic cases it may be subnormal. Anorexia, thirst, polyuria, dehydration and occasionally vomiting may occur. Polydipsia and polyuria are common. In toxic cases, nephritis with an elevated BUN will be noted. The white blood cell count in pyometra is usually elevated to over 50,000 cells per cmm and most of the leucocytes are neutrophils. The discharge from the vagina may be absent, scanty, or occasionally profuse. The discharge varies in color from yellowish-gray to reddish-brown and usually has a characteristic fetid odor. The degree of toxicity or dullness will depend upon the severity of the condition. Usually those cases with a closed cervix are more toxic than those in which a discharge is present. The pulse is usually elevated and rapid. The mucus membranes may be pale and in some chronic cases, anemia is present. The abdomen in some cases may be distended and pear-shaped. Palpation of the abdomen may reveal the distended uterus.

The course of pyometra is variable. Some cases become acute and severe within a week or two and require immediate and early attention to save the patient's life. In other cases, especially those with an open cervix from which pus is draining, the disease may run a course of a month or more. Frost reported on a strangulated inguinal pyometrocele in a bitch.⁹⁷ Bloom has reported on 2 cases of pyometra with unicornual uterine torsion.²⁵ He reported that in the cat a purulent peritonitis may occur secondary to pyometra, while in the dog a perimetritis, a parametritis or a peritonitis may occasionally develop. Remissions in the condition may be frequent in middle or late metestrus or early anestrus. Remissions would not occur in animals in which the cervix was obstructed by a tumor. A possible genetic relationship of obesity, diabetes mellitus and pyometra in certain breeds of dogs such as the Rottweiler and St. Bernard has been reported.¹⁵⁹

Treatment for pyometra, metritis, endometritis and

cystic endometrial hyperplasia in the non-breeding bitch and queen is ovariohysterectomy with supportive therapy consisting of systemic antibiotics, fluids and blood if necessary. Prior deep vaginal cultures with antibiotic sensitivity of the isolated microorganisms is important if post-surgical septicemia and peritonitis are present. *Escherichia coli* is most frequently isolated. In one study, 68 to 74% of the clinical cases were *Escherichia coli*.^{106,107} Other isolates include staphylococci, streptococci, *Proteus* spp., *Klebsiella* spp., *Salmonella* spp., *Pseudomonas* spp., *Pasteurella* spp., *Nocardia* spp. and *Mycoplasma* spp.^{106,107,136,165}

Animals with severe toxicity may be treated more conservatively with antibiotics, fluids, blood and prostaglandin therapy to promote drainage. With tranquilization and local anesthesia, the uterus can be marsupialized by suturing the uterus to the ventral abdominal wall and creating a fistula for drainage and local topical treatment until the bitch's condition improves and an ovariohysterectomy can safely be performed. Monitoring kidney function and other postoperative complications including peritonitis are important. Parenteral antibiotic therapy for 10 to 21 days may be necessary. Post-surgical uterine and ovarian stump granulomas and adhesions with sinus formations are the most commonly encountered lesions. Uterine and ovarian stump granulomas can usually be avoided by not using multifilament non-absorbable suture material including nylon, silk and linen for ligatures. Ligatures of 2-0 chromic gut showed no ovarian or uterine stump granulomas in 377 cases.²³⁸ Suture granulomas may result in abscessation, urinary dysfunction, partial bowel occlusion due to adhesions or fistulous tracts that may discharge into the vagina, paralumbar area, inguinal region, flank or medial aspects of the thigh.

Several investigators have reported on the clinical treatment of pyometra, metritis and endometritis with prostaglandin F₂ alpha.^{44,140,142,165,190,236,253} Prostaglandin F₂ alpha is very effective in causing luteolysis in late metestrus/diestrus or about 30 days post estrus, cervical dilatation and myometrial contraction. (see section on prostaglandins in Physiology of canine and feline Reproduction) It is highly effective in causing uterine evacuation in open pyometra, metritis or endometritis even when no corpora lutea are present. This condition is frequently seen in mismated bitches treated with estradiol. In the authors' experience, these bitches will frequently not have functional corpora lutea and only baseline levels of blood progesterone present (1 ng/ml). Usually within 24 to 96 hours after treatment with prostaglandin a great reduction in uterine size and an increase in myometrial tone can be palpated and vaginal discharge is abundant. The uterus will become quite rigid and de-

velop an irregular almost twisted or "ropey" feeling.¹⁶⁵

The subcutaneous median lethal dosage for PGF₂ alpha in the bitch is 5.13 mg/kg.²³⁷ Clinical signs of reaction and toxicosis include excessive salivation, emesis, diarrhea, hypernea, ataxia, urination, anxiety, and pupillary dilatation followed by constriction. Severity of side effects depends on the individual and are dose dependent. At low dosages, defecation is more frequent, while at intermediate dosages, hypernea, anxiety, hypersalivation, vomiting and defecation have been observed. Higher doses have caused ataxia and slight depression. The reported dose range has been from 0.02 to 1.0 mg/kg or 20 ug to 1000 ug/kg in the dog and 0.22 to 1.0 mg/kg or 220 to 1000 ug/kg in the queen administered intramuscularly or subcutaneously. Side reactions are seen in 20 to 120 minutes post-injection. Bitches appear to adapt with side effects diminishing by the fourth or fifth treatment. Cats appear to tolerate higher doses. Prostaglandins have not been approved for use in small animal medicine and should be considered as an experimental treatment by clinicians and owners of pets should be so informed.

The bitch has been reported to be treated for pyometra, metritis and endometritis with dosages of PGF₂alpha from 25 to 1000 ug/kg of body weight. Success has been obtained with single doses of 250 to 1000 ug/kg or with multiple injections of 25 to 250 ug/kg every 12 to 24 hours to effect. Daily single injections of 250 ug/kg have also been effective. Most of these dosage regimens were administered to effect (usually 3 to 5 days). Burke recommended a final dose be given 3 to 5 days after the initial treatment regimen to insure that the uterus is not refilling with exudate.⁴⁴ The author prefers to use a series of injections every 12 hours to effect. The dosage ranges from 25 to 250 ug/kg. The lower dosage is used first to evaluate the effect of the drug on each individual dog and to open the cervix and initiate mild myometrial contractions. The queen can be treated with the same dosage and regimen. Two queens with *E. coli* pyometritis were successfully treated with 200 ug/kg/day for 2 days and 500 ug/kg/day for 5 days along with oral administration of trimethoprim-sulfadiazine, 30 mg/kg bid for 30 and 21 days, respectively. Both cats were successfully bred and queened healthy litters.¹⁴⁰

Bitches and queens with pyometritis, metritis or endometritis were treated to effect with PGF₂alpha by the author.¹⁶⁵ Within 2 to 5 days, vaginal discharge was scant or absent and the uterus was reduced to a very firm small size. Parenteral antibiotics must be administered during PGF₂alpha treatment and continued for at least 10 to 30 days depending on the severity of the condition. If possible, antibiotic therapy should be initiated 24 hours prior to PGF₂alpha administration. Deep vaginal swabs for

bacterial, mycoplasma and ureaplasma culture and sensitivity should be taken to determine the most beneficial antibiotic therapy. Chloramphenicol is the drug of choice because it has a broad spectrum effect on several microorganisms and is highly effective against most strains of *E. coli*, mycoplasma and ureaplasma. Daily vaginal douches with 200 to 500 ml of a tepid 1% tamed iodine solution (**Betadine**, Purdue Frederick Co, Norwalk, CT) are beneficial in promoting vaginal drainage, cervical dilatation and uterine evacuation while systemic treatment of PGF₂alpha and a vulvar discharge is present. Daily abdominal palpation for size and consistency of the uterus, radiographs and the quantity of vulvar discharge should be used to determine the PGF₂alpha dosage regimen. This regimen has proven to be successful in both bitches and queens.

Several other medical treatments for pyometritis, metritis and endometritis in bitches and queens have been tried. These include the use of estrogens to open the closed cervix, oxytocin or ergonovine to cause uterine contractions and evacuation, indwelling uterine catheters to treat the infected uterus with various chemotherapeutic, antibiotic or disinfectant solutions on a daily basis, but none have been as effective as the combination of prostaglandins and antibiotic therapy.

The prognosis for medical treatment of this condition should always be guarded. The success rate decreases with age, degree of cystic degeneration, the development of microabscesses, adenomyosis, sacculated blind segments of the uterus, and endometrial polyps. The necrosis caused by an acute pyometritis or metritis is beneficial as it causes sloughing of the cystic endometrium. The author has been amazed that even older dogs that prior to this type of therapy would have been considered sterile have been treated successfully and are fertile. Young bitches, such as those that develop pyometritis or metritis secondary to an injection of estradiol for mating, will nearly all have a successful outcome following this therapy.

The most difficult condition to diagnose and treat is cystic hyperplasia of the endometrium. There are few overt clinical signs and the size of the genital tract makes it almost impossible to surgically or chemically or traumatically curettage the endometrium. Further investigations with fiberoptoscopes and chemical curettage may be indicated.

Successfully treated bitches and queens should be bred on the next estrus, especially those that are older and have had cystic endometrial hyperplasia. Recurrence of hyperplasia and reinfection are directly related to age and the number of non-productive estrous cycles. Following treatment, owners should watch for any sign of abnormal

vulvar discharge and/ or uterine filling. Deep vaginal swabs for culture and cytology should be obtained late in anestrus or early in proestrus to interpret the success of treatment and guide possible management and treatment prior to breeding.

Research in the prevention and treatment of this syndrome in the bitch and queen is needed. Prevention of non-productive estrous cycles is possible with the use of drugs for estrus control (see section in physiology on estrus control). Research on early luteolysis in non-bred dogs to eliminate the progesterone effect or physiological pseudopregnant state would be important. Good hygiene during breeding, whelping and postpartum care and routine genital tract examination will also decrease the incidence of this disease condition.

Miscellaneous Disorders of the Genital Tract

Miscellaneous disorders of the genital tract in dogs and cats include **endometrial polyps** which occur rarely in dogs and more commonly in cats as a further expression of cystic endometrial hyperplasia. These polyps may be single or multiple and can be the size of a fetus or larger. Many will have a small stalk attaching them to the uterine lumen wall. They are usually cystic, containing cystic endometrial glands. They can prolapse through the cervix and may also twist on their pedunculated stalk. This will lead to a bloody and/or mucopurulent fetid vulvar discharge. Vaginoscopic examination may reveal the prolapsed polyp and cause confusion concerning a differential diagnosis with a neoplasm. Large endometrial polyps can be palpated as a mass in the abdomen and radiographs following the infusion of soluble radiopaque fluid into the uterus using a Foley catheter in the anterior vagina during estrus or anestrus will reveal the polyps. The author has observed the death of a queen with an endometrial polyp following treatment for pyometritis with PGF₂ alpha. The polyp would not allow the evacuation of exudate through the cervix and exudate entered the peritoneal cavity via the oviducts resulting in a fulminating septic peritonitis. The author was also the prosector of a necropsy on a mature German Shepherd bitch that died suddenly (torsion) as a result of a unilateral torsion of a uterine horn containing a "potato-sized" endometrial polyp. The bitch died of acute hemorrhagic shock.

Adenomyosis, or the downgrowth of hyperplastic endometrial glands into the myometrium is also a sequela of cystic endometrial hyperplasia. The affected areas of myometrium appear as a firm tumor and is frequently confused with a leiomyoma or fibroid. On cut section,

the "swiss cheese" appearance of the cystic glands differentiate the condition from smooth muscle or fibrous tissue tumors of the myometrium.¹⁷⁶ A report of a 9-year-old Siamese cat with an enlarged abdomen and intermittent emesis was attributed to a 6×10.5 cm and 2 cm thickening of the body and horns of the uterus, respectively, and was diagnosed as adenomyosis.²⁰⁴ Large cysts or macroabscesses in the endometrium are secondary to obstruction of endometrial glands possibly secondary to inflammation in both dogs and cats.

Large serosal cysts or multiple serosal cysts may be seen in old multiparous bitches and are caused by trapping of the serosal epithelium in the involuting myometrium.¹⁷⁶ They are harmless and appear as multiple thin-walled cysts similar to cysticercus lesions caused by tapeworm larva. Lateral to the uterus, cervix and vagina, in the broad ligament in some females lie the remnants of the mesonephric ducts. If present, these may be cystic and be multiple or single cystic structures or long cystic tubules that can extend from the ovaries to the caudal vagina. The secretory lining epithelium of these **mesonephric cystic remnants** is stimulated by estrogen—progesterone of the estrous cycle.

Torsion of a uterine horn usually is associated with pregnancy, pyometra, endometrial polyps, hydrometra or mucometra or any condition that causes an increased uterine horn size.¹²⁶ A bilateral torsion of the right uterine horn of 1,080 degrees and the left uterine horn of 270 degrees was reported.²³⁵

Extrauterine pregnancies with or without severe ascites are a frequent finding in the cat. These may be incidental findings at the time of surgery or necropsy. Usually the mummified fetuses are adhering to abdominal organs or omentum. Some of these have been present for years and are mineralized masses. Extrauterine pregnancies may be either primary as a result of the zygote being dislodged from the oviduct and dropping into the abdominal cavity or intraabdominal fertilization, or secondary, as a result of uterine rupture. Most are secondary, although some have been reported as primary when attachment of fetuses to a blood supply have been found or when fetuses are found well after the time of ovariohysterectomy.^{29,180} Some believe that queens spayed at estrus or soon after, may have zygotes traumatically released into the peritoneal cavity that attach forming a blood supply and growing to a limited size before death.¹⁸⁰ The uterine horn should be examined closely for scars and adhesions, although the uterine horn will heal frequently without visible scars even following a caesarian section.^{75,221} (See pages 218 and 222)

Miscellaneous diseases of the genital tract in the queen include chronic vaginitis. Prepuberal vaginitis is

uncommon in the queen.^{63,167,239} Chronic vaginitis may be secondary to an open pyometritis or metritis, but more frequently is secondary to a dystocia or abortion and is caused by trauma of the cervix and/or vagina. The vulvar discharge is variable from scant and intermittent to abundant and continuous. It is usually mucopurulent. Vaginal examination with a small sterile otoscope (4 mm in diameter) following sedation or tranquilization of the queen may reveal a stenosis and fibrosis or scarring of the cervix and/or vagina. The prognosis is poor for any future breeding use of a queen with vaginal or cervical scarring. Ovariohysterectomy is advised. Vaginal cultures and cytology should be taken via the sterile otoscope head utilizing small 4 mm diameter sterile swabs and transport media for bacteria, mycoplasma, ureaplasma and viruses as described for the bitch earlier in this section. A specimen for cytology may also be obtained by flushing the vagina with sterile saline using a sterile eye dropper and aspirating the cells from the vagina. Abdominal palpation for evidence of pyometra should be carried out. Successful breeding following antibiotic therapy can occur if the birth canal is not damaged.

Several infectious diseases can cause fetal resorption, mummification, abortion, stillborns and teratogenic effects.^{63,132,167,239} These are discussed further under the section on diseases during gestation. These include feline viral rhinotracheitis, panleukopenia, toxoplasmosis, and ureaplasmas. Feline leukemia virus (FELV) and feline infectious peritonitis (FIP) have been associated with repeated services, poor conception, early embryonic and fetal death, resorption, abortion, mummification and stillborns in some catteries. Queens affected with these syndromes should be tested for evidence of FELV and FIP. Aborted fetuses, stillborns, portions of resorbed fetal material, placentas and vaginal swabs for culture should be submitted to a laboratory for both histological examination and culture for bacteria, mycoplasma, ureaplasma and viruses or fluorescent antibody detection of specific viral antigens.

Habitual and repeated abortion in some queens occurring always at the same time of gestation may be due to premature regression of corpora lutea of pregnancy or inability to successfully convert from luteal to placental progestogenic maintenance from day 45 to 50 to over day 60 of gestation. These queens should be checked for evidence of any infectious disease process and always be confirmed pregnant. Blood progesterone studies and ultrasonography for fetal viability throughout pregnancy would be of great scientific and clinical interest in these queens. A treatment consisting of intramuscular administration of repositol progesterone, 0.5 to 1.0 mg per lb.

beginning 7 to 10 days before the time of previous abortion and repeated at weekly intervals until 5 to 7 days before the anticipated date of parturition has been reported to be successful in some queens.^{167,239} Overdosage of progesterone may lead to masculinization of female kittens and prolonged gestation. The predisposition for this premature regression of corpora lutea of pregnancy and the inability to successfully carry fetuses to term may be inherited.

Subinvolution of Placental Sites

Subinvolution of placental sites (SIPS) results in a persistent or intermittent postpartum bloody vulvar discharge that continues longer than the normal discharge of postpartum lochia in the bitch. The etiology of this condition is unknown. Presumptive diagnosis is based on persistence of a sanguinous vulvar discharge beyond the normal postpartum discharge period. This may be continuous, or appear to be intermittent, with some indication that a heavier discharge may be seen postwhelping. A differential diagnosis must be made from metritis. Spontaneous recovery has been reported and in the author's experience, this can occur anytime between the normal postpartum lochial period to the next estrous period.

The first case report of subinvolution of placental sites was in 1966.²⁰ This condition was described and distinguished from other causes of persistent hemorrhage including normal postpartum lochia, postpartum endometritis or metritis, endometrial hyperplasia, urogenital tract neoplasia, trauma, urinary tract infections such as cystitis and pyelonephritis.

One or more or all of the placental sites may be affected. The placental sites that are involved appear from the serosal surface of the uterus as large ellipsoidal swellings, the diameter of the largest being about twice the size of the normal involuting site. The lumen or mucosal side of the uterus contains a small amount of blood-tinged fluid, sometimes large blood clots are present, and the affected placental sites are irregularly thickened, rough, and gray to brown, with areas of hemorrhage of various sizes. The myometrium over these sites is very thin, and in some the serosal area appears as a red or congested band around the uterus and may be quite friable or appears to be easy to rupture. The normal involuted placental sites after 9 weeks will show no ellipsoidal swellings on the serosal surface and on the mucosal surface only a brown color from hemosiderin laden macrophages will be seen at the placental site and the lumen site will be uniform in diameter and narrow. All reported cases

to date have been made from pathologic and/or histopathologic studies of tracts following ovariohysterectomy except for one case reported as a spontaneous recovery. (See page 345)

Normal and abnormal postpartum uterine involution of the bitch was studied and reported by Al-Bassam and co-workers.^{2,3} Of 95 reproductive tracts studied, 20 had subinvolution of placental sites. In this study, normal postpartum uterine involution occurred in 12 weeks and was considered complete when both placental and interplacental areas of the endometrium were covered by a single layer of small basophilic epithelial cells.

The gross description of **uterine involution** during these 12 weeks indicated that it was difficult to tell after 9 weeks that the normal uterus was not completely covered with an endometrial epithelium. During the first week postpartum, the uterus was dilated, edematous and showed signs of contraction on the serosal surface as longitudinal folds. The endometrial surface of the interplacental sites were covered with dark brown mucus, the placental sites were 1.5 to 2 cm in width and the surface was rough, granular and also covered with dark brown mucus and a few blood clots. During the second week, the uterus was smaller, the placental sites were visible from the serosal surface as swelling in the uterine wall. The entire mucosal surface was still covered by a dark brown mucus, but less in comparison to the first week. Placental sites were thicker and their surface was granular, grayish-tan and mixed with blood clots. By 4 weeks, the uterus was much smaller and the placental sites appeared on the serosal surface as ellipsoid swelling. The interplacental sites were less folded and covered with clear mucus. The placental sites were grayish-tan and contained 8 to 12 small grayish nodules and a few pinpoint hemorrhagic foci and blood clots were seen within the nodules. By 5 weeks the uterine horns were much smaller in diameter. The placental sites were small ellipsoid swellings. During the sixth and seventh week, the mucosal surface was light brown and narrow. About 6 to 8 grayish nodules were still present. By 8 weeks, the diameter of the uterine horn reached its smallest size. The uterine horns were uniform in shape and the placental sites were visible from the serosal surface as small ellipsoid shapes. Only a few grayish nodules were at the placental sites. By 9 weeks the uterine horns were uniform in shape with a narrow lumen; the placental sites were only differentiated from the interplacental endometrium by the brown color of hemosiderin filled macrophages.

Histologically, the plane of separation of the placenta at parturition usually lies in the distal portion of the spongy layer where there were only thin-walled partitions be-

tween the greatly dilated glands. Following placental removal, a necrotic mass forms over the basal glandular zone of the endometrium. This mass of eosinophilic staining material contains remnants of fetal placenta, fragments of the separated spongy layer, fibrin, erythrocytes, necrotic thrombosed blood vessels, nuclear debris, and large eosinophilic cells scattered in the upper loose connective tissue layer of the basal glandular zone and just under the necrotic mass. These cells are considered to be decidual maternal cells and/or trophoblastic fetal cells. The possibility of both being present is likely since some appear to be mostly nuclear with a binucleated nucleus similar to trophoblastic cells while others are highly secretory, with abundant eosinophilic granular cytoplasm similar to maternal decidual cells. The combination of both is quite possible since the presence of trophoblastic cells in the endometrium induces the formation of maternal decidual cells which are protective cells as well as a nutritional, secretory and possibly hormonal type cells. During the second week, collagen proliferation from the fibroblast in the lamina propria of the endometrium replaced the necrotic tissue. The necrotic debris was sloughed into the lumen of the uterus. This continued until maximum production of collagen was present in the placental site. A mononuclear cell infiltrate was present in the lamina propria at this time consisting of macrophages, lymphocytes and a few plasma cells. The surface over the collagen masses was still necrotic at this time and contained hemorrhagic areas. By the beginning of the 5th week, a massive sloughing of the collagen masses into the uterine lumen took place. Sloughing was to the level of the attachment of the endometrial lamina propria. This area was soon regenerated and covered by a single layer of columnar epithelial cells from the mouth and neck of the involuting uterine glands. By the end of 8 weeks, all of the collagen masses had sloughed and the entire placental sites were covered with a single layer of epithelium between 9 to 12 weeks postpartum. The interplacental sites, made up of hyperplastic endometrium containing primary and secondary folds, also became necrotic with complete loss of surface epithelium and formation of a necrotic surface. A collagen proliferation did not take place as in the placental sites. A complete single layer of new endometrial lining was produced from the mouth of the involuting glands. This process was also completed between 9 and 12 weeks postpartum.

From the above studies of Al-Bassam and co-workers, it appears that a bloody lochia in the normal bitch should persist for up to 3 to 4 weeks and then continue as necrotic debris, mucous and possibly old brown blood pigment until 7 or 9 weeks postpartum.

In their study of involutional abnormalities in the bitch, it appeared that trophoblastic-like cells invaded the endometrium and myometrium about 4 days postpartum in the bitch.³ These cells migrated along the spiral uterine arteries. This invasion or migration was similar to that seen in the human during the middle of pregnancy and in the golden hamster during gestation and up to 3 weeks postpartum. In the normal involutional process of the bitch, these retained fragments degenerated. In subinvolution of placental sites, these retained trophoblastic-like cells did not regress or degenerate, but continued to invade the deeper glandular layers of endometrium and even the myometrium. The presence of these cells caused necrosis of tissue around them, hemorrhage, and inability of blood vessels in this area to become thrombotic, occlude and degenerate. Early reports of this condition considered this condition as a chorioepithelioma or hydatid mole of the fetal placenta in the bitch (see previous section on neoplasia).^{2,15} Occasionally or rarely, the myometrium becomes so thin that rupture will occur, leading to hemorrhagic shock and peritonitis. The author has also studied 3 such cases in small breeds of dogs, 2 of these were Pugs and one a terrier, at or following delivery of their 2nd or 3rd litter. Rupture of the uterus took place either during parturition or the next day postpartum from old previous areas of subinvolved placental sites that had never healed yet one or more pregnancies had taken place. The uteri from these 3 dogs had multiple irregular raised areas on the serosal surface, most containing a green to brown pigmentation from old blood breakdown, that appeared to be proliferative lesions, but on examinations were very thin areas of the myometrium not covered by normal endometrium but covered only by a necrotic surface. No previous clinical history was given but it appears that these bitches could have had persistent or intermittent bloody postpartum discharge until the next breeding. New placental sites were located next to the unhealed placental sites. One report indicated that 8 of 26 dogs with histologically confirmed subinvolution of placental sites (SIPS) did not have a history of persistent sanguinous vulvar discharge suggesting that SIPS may be present in clinically normal dogs. The author has even diagnosed this condition in one bitch following elective abortion in late pregnancy with PGF₂ alpha.

The etiology of this condition is unknown. At one time, persistent corpora lutea of pregnancy or new postpartum corpora lutea producing luteal progesterone were implicated. This has been disproven since studies have shown that serum progesterone both in bitches with SIPS and in normal postpartum bitches is low and baseline even though in both, corpora lutea remain grossly visible for up to 12 weeks postpartum.^{2,3}

No histologic changes associated with bacterial infection or inflammation have been observed with subinvolution of placental sites. At one time, this was thought to be a condition affecting only first litter bitches, but further studies have shown that multiparous bitches can also be affected. Since many first litter bitches show signs of subinvolution of placental sites, it appears that prior uterine disease is not a major predisposing factor. There appears to be no breed predisposition or influence of eutocia or dystocia prior to clinical signs of subinvolution of placental sites. This condition usually occurs in bitches less than 3 years of age, but reports of histological confirmation ranged from 1 to 11 years.²

Clinically, subinvolution of placental sites is a complaint of bloody or serosanguinous vulvar discharge which persists longer or sometimes more abundantly than what is expected in the postpartum period. In most bitches, normal lochia or bloody mucus discharge has disappeared by 3 to 4 weeks postpartum. In bitches with clinical signs of subinvolution of placental sites discharge can continue for weeks and even into the next estrous period. The quantity of the discharge is variable and the character may range from serosanguinous to hemorrhage with blood clots and occasional visible necrotic debris. The discharge may be persistent or intermittent with some indication of a worsening condition at weaning or postweaning.⁶⁵ Affected bitches are usually normal clinically, bright, active, with normal temperature, pulse and respiration rates, a normal appetite and will whelp and raise their litters successfully. Occasionally a bitch may become weak and anemic especially those that have clotting disorders or poor health due to nutritional disorders, parasitic or other infectious diseases occurring with this condition. Occasionally a bitch will suffer uterine rupture from one of the affected sites resulting in hemorrhagic shock and peritonitis. Uterine size may be abnormal with spherical or elongated bands of enlargement up to 3 times larger in the affected site or sites to no detectable variation in uterine size on abdominal palpation. On laparotomy examination, the affected sites or zones are easily seen on the serosal surface as being enlarged, thinned and congested or red to brown in color. Vaginal cytology will reveal abundant red blood cells, necrotic debris, variable amounts of mucus, a few non-cornified round epithelial cells and scant polymorphonuclear leukocytes. If an endometritis or metritis is present, the vaginal smear would also contain abundant numbers of toxic polymorphonuclear leukocytes and bacteria. The bitch would also show clinical and systemic signs of an inflammatory condition. Vaginoscopic examination would reveal a hemorrhagic discharge from the cervix. Vaginoscopic examination with air insufflation in the

first 2 or 3 weeks and possibly later postpartum will reveal the cervix relaxed and open and the ability to view the placental sites. Caution not to cause trauma with the scope is important. With the use of a Foley catheter, soluble sterile radiopaque solution can be placed in the uterus and then evacuated. After 1/2 hour the placental sites can be viewed radiographically. This procedure should not be done until vaginal cytology and vaginoscopic examination indicates that endometritis or metritis are not present. The most definitive diagnosis is to biopsy the affected area via laparotomy. The most practical approach is to rely on clinical history and vaginal cytology, deep vaginal culture and vaginoscopic examination in making a clinical diagnosis.

Ovariohysterectomy is the best treatment in bitches with SIPS not intended for future breeding use. Spontaneous recovery has been reported in one bitch and the author has seen other cases spontaneously recover, some within a few days following the examination of the genital tract with vaginoscopy and insufflation procedures. Possibly this manipulation had some effect. Use of oxytocin, ergonovine or prostaglandins by the author in treating bitches with subinvolution have not altered this condition. A study was reported of the successful treatment of 10 cases of persistent postpartum uterine hemorrhage in the bitch with a single subcutaneous dose of 25 to 50 mg, 2 mg/kg of bodyweight, of medroxyprogesterone, MPA (**Depo-Provera**, Upjohn Co., Kalamazoo, Mich.). Vulvar discharge was reported to disappear by day 3 posttreatment, and 4 of the 10 bitches were bred at the next estrus, conceived and whelped normal litters of pups.⁸ This appears to be the only successful medical treatment report to date. The product, medroxyprogesterone acetate, is the same product that caused many pyometras following its use as an injectible contraceptive in the U. S. during the 1950's, but has continued to be used very successfully in Europe and appears to be safe at this time period in the bitch as long as there is no indication of inflammatory conditions such as endometritis or metritis.

There are clinical impressions by some breeders and veterinarians that post-whelping oxytocin injections prevent the development of subinvolution of placental sites. Certainly this practice should be encouraged not only because of this clinical impression, but it does help with uterine evacuation of retained dead pups and/or placentas, controls uterine hemorrhage and initiates milk let-down. Either one or two injections 12 to 24 hours apart, with the first given after the bitch appears to have finished whelping, are administered either intramuscularly or subcutaneously. Hysterolaparotomy and gentle curettage of affected endometrial sites has been considered in selected valuable breeding bitches. The success of this

treatment has not been studied. Blood transfusions and selected antibiotic therapy may be needed for the anemic patient or the patient that develops endometritis or metritis.

Further research is needed to determine the incidence of subinvolution of placental sites, its effect on future fertility, the possibility of a genetic predisposition, and successful methods to prevent or treat this condition.

Breeding Soundness Examination

Several excellent reports on **breeding soundness examinations** and diagnosis and therapeutic approaches to infertility in the bitch^{143,149,164,166,200,213,233,246} and the queen^{43,60,63,112,121,151,167,239} are available and the author encourages the reader to review these articles further. The veterinary student, practicing veterinarian and owner of breeding dogs and cats must fully understand the normal reproduction cycle and physiology of these animals before they can understand infertility problems. A detailed history, thorough urogenital tract examination and general physical examination of the bitch and queen are indicated for a fertility examination. The history should include fertility and breeding history of the bitch or queen, littermates and maternal and paternal records if available. The breeding record of males used should also be evaluated. Genetical problems are better appreciated if pedigrees are available. General health records, diets, feed and management practices in kennels or catteries should be obtained. Psychological and environmental stresses are important in some breeding problems. The use of the animal is important, especially if showing, racing or field performance and competition are a part of the animal's activities. All breeding dogs should be routinely blood tested for **Brucella canis** and infertile bitches and stud dogs should be tested for thyroid and adrenocortical function. All breeding queens should be blood tested for evidence of feline leukemia and feline peritonitis virus. A complete physical examination for general health, a hemogram, and a complete urogenital tract examination, including vaginoscopy, vaginal cytology and palpation of the urogenital tract per vaginum, rectum and abdomen should be carried out. Vaginal cultures need only be done on infertile females. Bitches and queens with estrous cycle problems should be followed through these cycles as characterized by sexual behavior, vaginal cytology and possibly hormone profile testing for progesterone levels. Bitches and queens with poor conception or possible early embryonic or fetal death and abortion problems should be followed throughout breed-

ing and pregnancy with vaginal cytology, cultures, progesterone blood levels, pregnancy diagnosis and if possible fetal viability utilizing ultrasonography. Diagnostic methods utilizing radiography for late fetal death and hysterosalpingography utilizing soluble radiopaque fluid for detecting genital tract abnormalities and pathology are available.^{61,62,169} Laparoscopic studies of the urogenital tract and biopsy of the uterus may be indicated for further diagnosis. Excellent records, a systematic approach to examinations, clinical tests and follow-up visits, and an educated and informed pet owner knowledgeable concerning normal reproductive physiology and common problems of their bitch or queen are all necessary to a successful breeding program.

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Chapter XVIII

INFERTILITY IN MALE ANIMALS (Andrology)

It is probable that infertility or sterility is as common in the male as in the female. Because of the greater hazards presented by parturition and pregnancy, acquired infertility or sterility is much more frequent in the female. The degree of fertility in males may vary greatly but is more easily evaluated because of the large numbers of females bred by each male, especially those males used in artificial insemination. Thirty-six to 48 percent of dairy and beef bulls used in artificial insemination are slaughtered for low breeding efficiency.^{1,2,5,6,7} Probably many of these would have provided satisfactory natural service. Only 28 percent of nearly 9,000 dairy sires used artificially were useful at 10 years of age and older. Arthritic diseases resulting in inability to copulate or reduced libido was the most frequent cause for culling of older bulls. A report of the Jockey Club showed a great range in fertility in Thoroughbred stallions with an average conception rate of 57 percent for all stallions.³ This survey considered the fertility of both the stallion and his mares. Further information on the incidence of male infertility was reported by Laing.⁴ Probably less than 0.5 percent of male animals with normal appearing testes and penis are completely sterile. However there exists a wide variation between males in their fertility.

Because the male genital organs can be readily examined and semen examination by means of the artificial vagina, or by electroejaculation in nearly all domestic animals is easily accomplished, many aspects of male infertility have been studied. With the rapid advances made in artificial insemination in recent years has come a greatly increased knowledge concerning male infertility. Whenever a serious infertility problem with a marked drop in conception rate occurs in a group of females, the male or the semen is always to be suspected until proven otherwise. The selection of males for sires should be done very carefully from the genetic standpoint since the male is responsible for 50 percent of the genes present in his daughters, after 3 generations the sires used in a herd are responsible for 88 percent of the genes in the females.

When any genital organ becomes severely impaired by

disease, it usually cannot be restored to its ideal physiological state. For this reason one must look with extreme skepticism on cures claiming a high rate of complete recovery. The prognosis in treating sterility or infertility in males should always be guarded. There is increasing evidence that the genetic make-up of a sire largely determines his fertility and potency. Only severe diseases, nutritive deficiencies, aging effects or injuries have important or lasting effects on male fertility. There is usually little that treatment or therapy can do to significantly improve the level of fertility in a congenitally infertile male.

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The Anatomy of the Testes and the Male Genital Tract

The **scrotum** is present in all the domestic animals and encloses the testes. The scrotum of the domestic animals with the exception of the boar and tom is located between the thighs. In the boar and tom the scrotum is located caudal to the thighs and caudal and ventral to the ischiatic arch. It is composed externally of skin that is relatively free of hair except in toms, rams and bucks.

Beneath the skin is the **dartos** consisting of fibro-elastic tissue and unstriated muscle. The dartos is connected closely with the **tunica vaginalis** and the remnant of the gubernaculum forming the **proper ligament of the testis** and the **ligament of the tail of the epididymis**.⁷ The testis and epididymis are fixed in the scrotum by means of these ligaments and the **mesorchium**. The latter is a long serosal fold of peritoneum, like the mesentery, extending from the lumbar region to the tail of the epididymis and between the tunica vaginalis parietalis and the epididymal border of the testis adjacent to the ductus(vas)deferens.²¹ The scrotum has a medial septum formed by the dartos dividing the scrotum into two halves. The **spermatic or scrotal fascia** is fastened by loose areolar tissue to the dartos and this fascia is lined by the **tunica vaginalis parietalis (communis)**, a fibro-serous sac continuous with the parietal peritoneum. The tunica vaginalis is thin above, but thicker in the scrotum. The scrotum, **cremaster muscles**, and the **pampiniform plexus** regulate the temperature of the testes, keeping it lower than body temperature. The marked contractibility of the scrotum, causing wrinkling in cold weather, is due to the dartos and cremaster muscles.

The principal blood supply to the scrotum is the **external pudendal artery** and also the internal pudendal artery in the boar and tom. Innervation of the scrotum is by means of the genital nerve, a branch of the genitofemoral nerve arising from the second to fourth lumbar nerves and the perineal nerve. The smooth muscle of the scrotum is supplied by the spermatic plexus from the pelvic plexus of nerves.

The testis is supported in one of the two scrotal pouches where it is held by its tunics and by the **spermatic cord**, the latter is composed of the following: the **spermatic artery** tortuously coiled just dorsal to the testes; the **spermatic veins**, which form a plexus of veins, the **pampiniform plexus**, around the spermatic artery; the **internal cremaster muscle**; lymphatic vessels and the **autonomic nerves** from the renal and posterior mesenteric plexuses which form the spermatic plexus around the vessels in the cord, the **ductus deferens**, and the **tunica vaginalis (propria)**. The distal end of the testis is attached to the scrotum by the scrotal ligament, except in the bull.

The **testis proper** is closely covered by a thin serous membrane, the tunica vaginalis (propria). Beneath the structure is a dense, thick connective tissue capsule, the **tunica albuginea**, from which, except in the stallion, septa radiate to the **mediastinum testis** to form the lobules of the testis. Within these lobules are the **seminiferous tubules**, comprising 70 to 90 percent of the weight of the testis. These tubules are lined by germinal epi-

thelium that produces spermatozoa. The length of these seminiferous tubules has been estimated to be: for the boar 6,000 meters, the bull 5,000 meters, the ram, 4,000 meters, the dog 150 meters, and the tom 25 meters.⁵ Between the seminiferous tubules are islands of **interstitial or Leydig cells**. The seminiferous tubules converge at the apex of the lobule at the receptacle,¹⁷ to join the tubuli recti, or straight tubules that enter the **rete testis**, a structure of anastomosing spaces located in the mediastinum testis. The rete testis is most highly developed in the stallion of the domestic animals.¹ There is no mediastinum testis in the stallion, as is present in the other animals, and the equine collecting tubules join the efferent tubules. From the rete testis the sperm passes to the **head of the epididymis** through 13 to 20 **efferent tubules** or ducts.¹⁴ The **testicular artery** enters the testis from the spermatic cord and passes to the distal end of the testis before sending branches through the tunica albuginea and the substance of the testis. The veins, small at the distal end, tend to enlarge as they unite at the proximal or spermatic cord end of the testis. On examination of the testes the tortuous configuration of blood vessels is most readily noted in the tunica albuginea in the bull. This is a further provision assisting the **heat regulatory mechanism of the testis**. The consistency of the testis is usually turgid. The parenchyma is yellow to reddish brown in color and bulges on section.

The **epididymis** is composed of a single, tortuous, coiled tubule that is essential for the transportation, nutrition, storage, and maturation of the spermatozoa. It has a smooth muscle coat that moves the sperm in peristaltic waves toward the ductus deferens. Much absorptive and secretory activity occurs in the epididymis. The length of the epididymal tube is about 30 meters in the bull, 50 meters in the boar and 20 meters in the horse.¹¹ The proximal or spermatic cord end of the epididymis is more or less flat, broad and U-shaped; and is called the **head of the epididymis**. The intermediate narrow part is called the **body**, and the distal enlarged end, which acts as a storage site for spermatozoa, is called the **tail of the epididymis**. This is continuous with the **ductus deferens**. The epididymis is closely attached by fibrous tissue to the surface of the testis proper.

The **testis of the bull** is oval in shape, about 10 to 15 cm. long and 5 to 8.5 cm. in diameter and weighs about 200 to 500 gm. The long axis of the testis is vertical and the body of the epididymis lies caudal and medial to the testis. The head of the epididymis is dorsal and the tail ventral to the testis. The ductus deferens lies parallel to the body of the epididymis and medial and cranial to it.

The **testis of the stallion** is oval in shape but slightly compressed from side to side, about 7.5 to 12.5 cm.

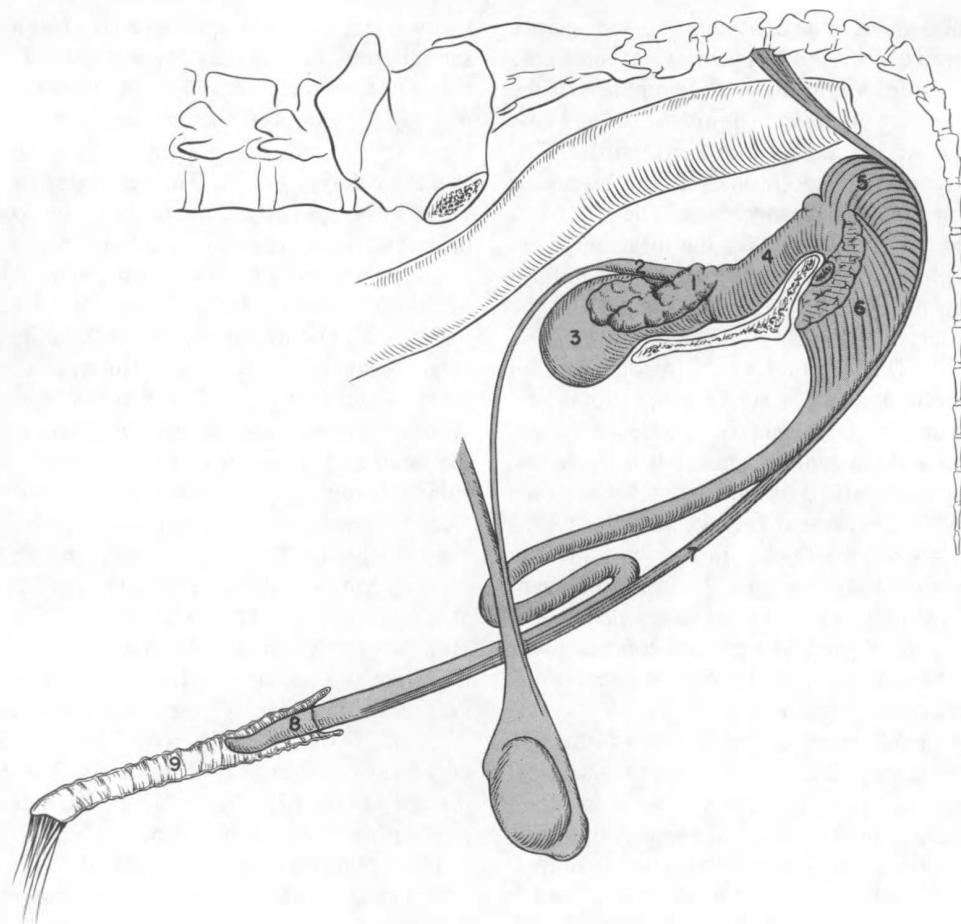


Figure 159. The Genital Organs of the Bull. 1. Seminal Vesicle 2. Ampulla of the Ductus Deferens 3. Bladder 4. Urethral Muscle Surrounding the Pelvic Urethra 5. Bulbocavernosus Muscle 6. Ischiocavernosus Muscle 7. Retractor Penis Muscle 8. Glans Penis 9. Preputial Membrane and Cavity.

long, 4 to 7 cm. dorsal-ventrally and about 4 cm. thick. It weighs about 200 to 300 gm.^{1,12,19} The long axis of the testis is nearly horizontal. When the testis of the stallion is retracted it becomes nearly vertical. The tail of the epididymis is caudal and loosely attached to the testis. The body lies dorsal to the testis with the head of the epididymis cranial. The ductus deferens lies dorso-medial to the body of the epididymis and testis. The horizontal plane of the testis makes torsion of the testis possible in the stallion and dog, although it occurs only rarely. The **appendix testis** is nearly always present as a small protruding structure on the cranial pole of the equine and ovine testis. It is a remnant of the paramesonephric duct.

The **testis in the ram and the buck** is oval in shape 7.5 to 11.5 cm. long and 3.8 to 6.8 cm. in diameter and weighs 200 to 400 gm. The plane of the testis is similar to that in the bull.

The **testis in the boar** is oval in shape, 10 to 15 cm.

long and 5 to 9 cm. in diameter. The testis of mature boars weigh between 500 to 800 gm. with an average of 600 gm.^{9,18,21} The long axis of the testis is almost vertical. The free border of the testis is caudal. The tail of the epididymis is dorsal, the body cranial and the head of the epididymis ventral. The tail of the epididymis is quite large. The ductus deferens lies cranial and medial to the testis. The spermatic cord is long.

The **testis of the dog** is similar in location to the testis of the stallion, but lies slightly more obliquely. The tail of the epididymis is caudal and the head cranial. The testis of the dog is small, about 2 to 4 cm. in length and 1.2 to 2.5 cm. in diameter. The dog testis weighs about 7 to 15 gm.^{10,12,19}

The **testis of the tom** is similar in location to the testis of the boar. It is small, 1.2 to 2 cm. in length and 0.7 to 1.5 cm. in diameter.

The **inguinal canals** of domestic animals are well de-

scribed.³ There are marked species differences. The dog and bull are similar to the boar with large deep inguinal rings and short inguinal canals, while the stallion has a small deep inguinal ring and a long inguinal canal. The canal is a slit like space between the deep inguinal ring and the superficial inguinal ring formed by the tendon of the external abdominal oblique muscle.

The **ductus (vas) deferens** extends from the tail of the epididymis to the colliculus seminalis of the pelvic urethra. The wall of the ductus is thick and the lumen quite small. It passes parallel to the testis, into the spermatic cord, through the inguinal canal in a fold of the vaginal tunic and dorso-medially to the neck of the bladder in the medial edge of the genital fold. From its origin to the dorsal surface of the bladder the ductus deferens is of a uniform thickness of about 3 to 6 mm. in diameter in the bull and stallion, respectively. The fusiform enlarged terminal glandular portion of the ductus is called the **ampulla of the ductus deferens**. In the bull it is 10 to 12 cm. long and about 1 to 1.5 cm. in diameter, and in the stallion 15 to 20 cm. long and about 2 to 2.5 cm. in diameter. A distinct ampulla is not observable in the boar, dog or tom although luminal alterations are present. The ampullae in the bull lie dorsal to the neck of the bladder parallel to each other and in close apposition. Caudally the ampullae narrow and pass under the body of the prostate and open through a rounded prominence, the **colliculus seminalis**, into the cranial portion of the **pelvic urethra**. One or both ampullae may be entirely dorsal, entirely ventral, or intermediate in position to the vesicular glands in the bull.⁷ The blood supply of the ductus deferens is the testicular artery and internal pudic artery. The nerve supply is from the pelvic plexus.

The **accessory male genital glands** include the vesicular glands (seminal vesicles) the prostate and the bulbourethral glands. The **vesicular glands** (seminal vesicles) are paired accessory genital glands of the male located on the floor of the pelvis, cranial and lateral, to the ampullae and neck of the bladder. The lobes of the vesicular glands have small central dilatations in ruminants and the boar but a large central dilatation in the stallion.^{1,19} In the stallion, because the structure is more bladder-like with the glands in the walls, it is still called the **seminal vesicle**.²⁰ These glands secrete a clear fluid that adds volume, nutrients and buffers to the semen. They open into the pelvic urethra in close proximity to the openings of the vasa deferentia. They do not store spermatozoa. The vesicular glands are absent in the dog and tom. In the bull the vesicular glands are lobulated, 10 to 15 cm. long, and 2 to 4 cm. in diameter. In the stallion the seminal vesicles (vesicular glands) are smooth, 15 to 20 cm. long and about 2.5 to 5 cm. in diameter.

In the boar the vesicular glands are proportionately very large, 10 to 15 cm. long, 5 to 8 cm. wide and 5 to 8 cm. thick. They cover the caudal portion of the bladder and extend into the abdominal cavity. A portion or much of the vesicular glands are covered with peritoneum in the bull, stallion, boar and ram. The vesicular glands of the ram and buck resemble those of the bull.

The **prostate gland** has variable forms in all domestic animals but is located on the floor of the pelvis, caudal to the bladder and on or around the neck of the bladder where it is closely fused with the pelvic urethra. It adds its secretions to the semen at the time of ejaculation by means of many ducts opening into the pelvic urethra lateral to the colliculus seminalis.

In the bull the body of the prostate gland is 2.5 to 4 cm. wide and 1 to 1.5 cm. thick. It can be felt per rectum as a distinct transverse protuberance on the cranial end of the pelvic urethra. The **pars disseminata of the prostate gland** surrounds the pelvic urethra. Dorsally it is about 1 to 1.5 cm. thick and 10 to 12 cm. long and is covered by the urethral muscle. In the ram and buck the prostate gland has no body only the disseminate portion diffused over a large area of the pelvic urethra.

In the stallion the prostate gland is situated over the neck of the bladder and cranial portion of the urethra. It consists of two lateral lobes connected by an isthmus. Each lobe is about 5 to 9 cm. long and 2.5 to 6 cm. wide. There is no disseminate portion.

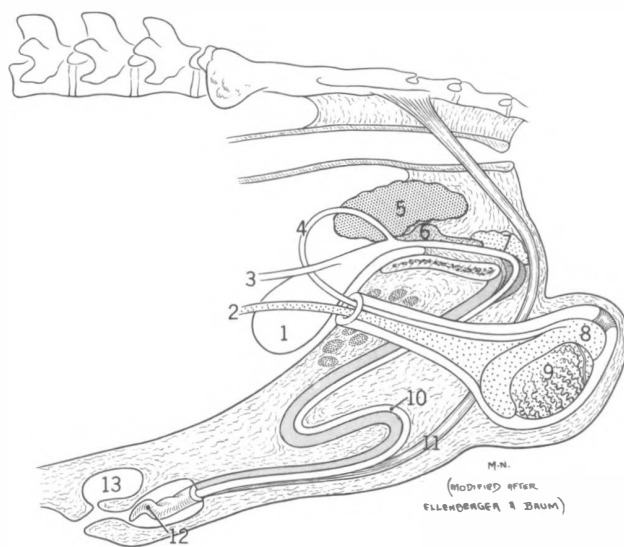


Figure 160. The Urogenital System of the Boar. 1. Urinary Bladder 2. Spermatic Vessels and Nerves 3. Ureter 4. Ductus Deferens 5. Vesicular Gland 6. Prostate 7. Bulbourethral Gland 8. Tail of the Epididymis 9. Testis 10. Urethra 11. Retractor Penis Muscle 12. Glans Penis 13. Preputial Diverticulum.

In the boar the body of the prostate gland is located dorsal to the bladder and is covered by the vesicular glands. As in the bull and ram the disseminate prostate gland around the pelvic urethra is quite extensive.

In the dog the prostate gland is relatively large and composed of rounded left and right lobes which lie at the cranial border of the pubis. It surrounds the neck of the bladder and urethra at their junction and is thin dorsally. The excretory ducts are two in number. The size of the gland varies greatly and may be quite enlarged in older dogs. In a 2 to 5-year-old, 25-pound dog it may vary from $1.7 \times 2.6 \times 0.8$ cm. to a near perfect sphere 2 cm. in diameter weighing about 7 gm.^{10,19} A few disseminate lobules of the prostate gland are present in the wall of the urethra. The prostate of the tom is similar to the dog except it does not cover the ventral part of the urethra.

The **bulbourethral (Cowper's) glands** are paired glands lying dorsally on either side of the pelvic urethra near the ischiatic arch. They are generally ovoid in shape. In the horse they are about 2.5 to 5 cm. in diameter. In the bull they are slightly smaller than in the stallion. In the ram and buck the bulbourethral glands are relatively large, 0.5 to 1 cm. In the boar the bulbourethral glands are large, dense, and cylindrical in shape about 12 to 18 cm. long and 2.5 to 5 cm. in diameter and lie on either side of the pelvic urethra. In the dog the glands are very small, about 5 mm. in diameter.¹⁹ In the tom the bulbourethral glands are nearly as large as the prostate gland. These glands have 3 to 4 excretory ducts each, opening into the urethra in the stallion.¹⁹ But only a single duct from each gland is present in the bull, boar, ram and tom. In ruminants these ducts open under a fold of mucous membrane in the dorsal wall of the urethra. This blind pouch or diverticulum at the ischial arch prevents the passage of a urethral catheter or probe into the bladder.^{12a,14b} In the castrated male the accessory glands and the penis are small and undeveloped.

Urethral glands, although prominent and numerous in man, are not present in the bull, stallion, dog and tom. The pelvic urethra in the bull, ram, buck and boar contains many glands similar to those in the prostate gland and this diffuse layer of glands is correctly called the disseminate part of the prostate gland and should not be called "urethral glands."^{16,20}

The blood supply to the accessory glands in the larger domestic animals is the internal pudental artery. In the dog it is the prostatic artery, a branch of the urogenital artery arising from the internal iliac artery.¹⁰ The nerve supply is by autonomic nerves from the hypogastric nerve and pelvic plexus.

The **uterus masculinus** is a rudimentary structure, a

remnant of the paramesonephric ducts, situated on the caudal dorsal surface of the bladder between the ampullae of the ductus deferens and the vesicular glands and cranial to the prostate. (See Figure 161.) Its presence, size, and development are variable. The uterus masculinus was found in 50 to 70 percent of the bulls examined.⁷

The **penis** is the copulatory organ of the male. It is more or less cylindrical in form in all species. It extends forward from the ischiatic arch to the umbilical region on the abdominal wall except in the tom. It is supported by the penile fascia and skin. Prescrotally it is situated in the **prepuce or sheath**. The terminal portion of the penis is called the **glans** and this lies free in the prepuce. The **body of the penis** is composed of a right and left **corpus cavernosum penis** (enclosed by a thick fibrous capsule, the **tunica albuginae**) and a **corpus spongiosum penis** surrounding the urethra. The corpora are spongy in character and divided into many cavernous spaces. They are continuous with the veins of the penis. Erection of the penis is caused by a distention of these spaces with blood.

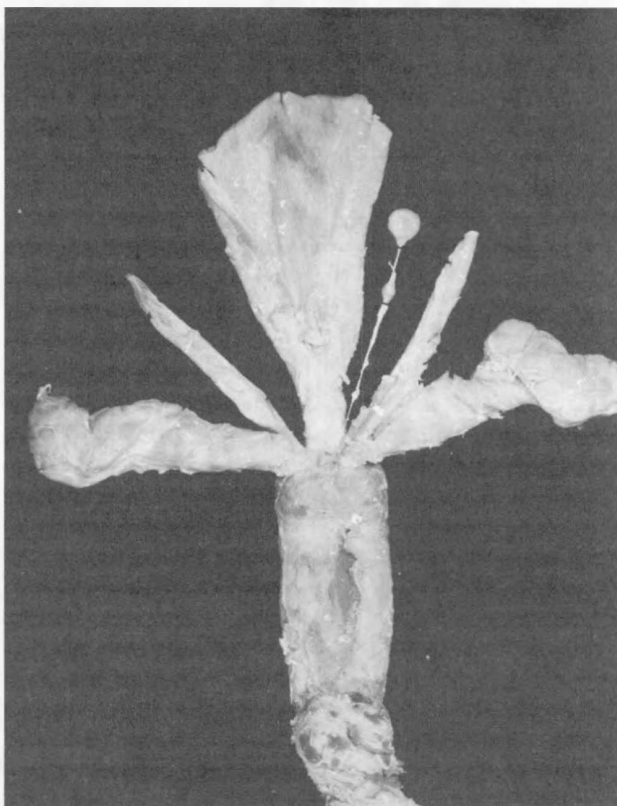


Figure 161. The Uterus Masculinus in a Bull (It is usually located between the ampullae and dorsal to the bladder).

The boar and ruminants have a fibroelastic penis in which the trabeculae predominate over the cavernous spaces; while in the stallion and dog with a musculo-cavernous penis the reverse is present. Thus in the non-erect state the former animals have a firm penis while the latter have soft compressible penis.¹⁹ The root of the penis is formed by two **crura** that fasten the penis to either side of the ischiatic arch. The **ischo-cavernosus muscle** arises from the tuber ischii and is inserted on the crus and body of the penis. It causes erection by its compressing and pumping action on the bulbous portion of the corpus cavernosum penis underlying the muscle. The **retractor penis muscle** is a combination of striated and smooth muscle which arises on the first and second caudal vertebrae, receives some fibers from the anal sphincter and meets again under the anus. This paired muscle passes along the ventral caudal surface of the penis and attaches to the tunica albuginea of the penis. In the boar and ruminants the retractor penis muscle is inserted on the distal curve of the sigmoid flexure. Its action is to return the penis into the prepuce after erection.

The muscles of the **pelvic urethra** include the urethral muscle, which is a circular muscle consisting of dorsal and ventral layers of transverse fibers. By its forcible contraction it aids ejaculation and micturition. The **bulbospongiosus muscle** is a thick circular muscle and is a continuation of the urethral muscle on the extrapelvic urethra. It is thickest at the root of the penis. It empties the **extrapelvic urethra**.

In the stallion this muscle, enclosing the ventral portion of the urethra extends to the glans as does the retractor penis muscle.^{1,19} The blood supply of the penis is the **internal pudendal artery** in the boar and ruminants while in the stallion, dog and tom this artery and the external pudendal and obturator arteries also supply the penis. The nerves to the penis are the autonomic nerves of the pelvic plexus and the pudendal and hemorrhoidal nerves. These latter nerves are the motor nerves of the retractor penis muscle. The sensory fibers to the glans penis come from the **dorsal nerve of the penis**, a branch of the pudendal. The glans penis is plentifully supplied with nerves and nerve endings.

The **penis of the bull** is characterized by an S-shaped curve, or **sigmoid flexure**, caudal and dorsal to the scrotum. The penis in the adult bull is approximately 90 cm. long from the root to the tip of the glans. The erectile tissue is small in amount as compared to that of the stallion. The penis of the bull in the erect state is seldom over 4 to 5 cm. in diameter. The glans penis is about 7.5 to 12.5 cm. long, rather pointed and twisted slightly counterclockwise.¹⁹ During erection the S-curve is obliterated.

Bos indicus bulls have greater total penis length and prepuce length than **Bos taurus** breeds, 111 vs 105 cm. and 55 vs 49 cm., respectively. This may be related to the higher incidence of prolapse in the former breeds.^{6a} The well-developed retractor penis muscle attaches to the penis at the cranial or distal end of the sigmoid flexure with fibers extending dorsally on the penis to near the glans to unite with the fibrous tunic surrounding the distal 7.5 cm. of the corpus cavernosum. The thickened dorsal portion of this fibrous sheath is known as the **dorsal apical ligament** of the penis.⁴ At the time of erection and service the penis is protruded 25 to 60 cm. out of the prepuce.

The **penis of the stallion** has a large amount of erectile tissue. In the nonerect state it is about 50 cm. long and 2.5 to 6.0 cm. in diameter; 15 to 20 cm. lies free in the prepuce. At the time of erection the penis will double its length and thickness, with the glans penis enlarging three or more times its quiescent size. Dorsal to the **urethral process** of the glans penis is the **urethral sinus, or diverticulum**, which is sometimes filled with inspissated smegma which is called the "bean." The retractor penis muscle is not as strong as in the bull. No sigmoid flexure is present.

The **penis of the ram and buck** is characterized by a **urethral process** extending 4 to 5 cm. beyond the glans penis. The glans penis is 5 to 7.5 cm. long. The diameter of the penis in the ram is relatively small, 1.5 to 2 cm. The ram's and buck's penis is about 30 cm. long with a well-developed sigmoid flexure.

The **penis of the boar** is similar to the bull but the sigmoid flexure is prescrotal. The cranial portion of the penis which has a small glans is spirally twisted counterclockwise.^{19,21} The penis is 45 to 55 cm. in length and at the time of copulation about 20 to 35 cm. protrudes beyond the preputial opening.

The **penis of the dog** has in its caudal part two distinct corpora cavernosa separated by a median septum. The length of the non-erect penis in the dog is 6.5 to 24 cm. In the cranial free portion there is bone, the **os penis**, which varies from 5 to 10 cm. in length depending on the size of the dog. This bone is thick proximally and tapers distally. Ventrally this bone is grooved for the urethra. A penile bone is also present in other carnivores. The **glans penis consists of two parts**, the **pars longa glandis**, the distal or cranial two-third of the glans, averaging 5.3 cm. in length, and the **bulbus glandis**, the proximal one-third of the glans, averaging 2.4 cm. in length and about 2 cm. in diameter. The bulbus glandis expands greatly at the time of erection and prevents withdrawal of the penis from the vestibule of the bitch during ejaculation. The canine penis during coitus has

been well-described as a "paradox of flexible rigidity"^{12b} since during coitus the male usually dismounts and faces in the opposite direction.

The **penis of the cat** is short and is directed caudally and downward. The urethra is located dorsally. The os penis which is 3 to 5 mm. long is located distally. There is no glans penis, but merely a **terminal cap** about 1 cm. long that contains numerous, about 120 **papillae or spines** pointing toward the base of the penis.² These spines are a secondary sex characteristic. It is questionable that these cause the queen to cry out on intromission. In the tom the bulbus glandis is absent.

The **prepuce, or sheath**, is a double invagination of skin which contains, and is much longer than, the free portion of the penis when not erect. It covers the body of the penis behind the glans when the penis is erect. The external opening of the prepuce is called the **preputial orifice**. The penis of domestic animals lies against the ventral abdominal wall. The body skin covers the prepuce ventrally. The lining of the prepuce is a freely movable membrane or modified skin that is attached firmly only at the glans penis and the preputial orifice. The blood supply of the prepuce is branches of the external pudendal artery and the innervation is from the pudendal ilio-hypogastric, and ilio-inguinal nerves.

The **prepuce in the bull** is long and narrow, 35 to 40 cm. in length and 4 cm. in diameter. The preputial orifice is about 5 to 7 cm. behind the umbilicus and is small, 2 to 4 cm. in diameter, and surrounded by a tuft of long preputial hairs. There are usually two pairs of cranial and caudal **preputial muscles**, protractors and retractors, that draw the preputial opening either forward or backward. The **fornix** of the sheath in the bull is the point at which the prepuce reflects upon the penis just caudal to the glans.

The **prepuce in the stallion** has a preputial cavity extending caudally from the preputial orifice 15 to 20 cm. deep and 6 to 10 cm. in width and then a second reflection or annular fold of prepuce to form the second, more caudal cavity with a narrower lumen surrounding the free portion of the penis, **prepuce proper of the penis**. The opening between these two cavities is called the **preputial ring**. The engaging and disengaging of the glans penis in the preputial ring causes the sucking noise frequently heard when the gelding or stallion trots. The secretion of the preputial glands and epithelial debris causes the formation of **smegma** in the sheath of the horse and males of other species.

The **prepuce of the ram and buck** is similar to the prepuce of the bull but is relatively not as long.

The **prepuce of the boar** has a small orifice with long bristle-like hairs. The caudal part of the prepuce is narrow and the cranial part wide. In the dorsal wall of the

wide part is an opening that leads into the **preputial diverticulum**. This, when filled with urine, semen and smegma, can resemble an umbilical hernia.

The **prepuce in the dog** has a small preputial orifice and a relatively long cavity extending to the bulbus glandis. The **prepuce of the tom** consists of a short fold surrounding the caudally directed preputial orifice.¹⁹

Swine and ruminants tend to urinate inside the prepuce, whereas stallions, dogs and toms extend the penis beyond the sheath. Bucks may extend the penis beyond the prepuce and urinate during courtship of a doe. In ruminants and swine castrated before puberty, the prepuce remains firmly attached to the glans penis, as it is in the prepubertal state.

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The Embryology of the Male Reproductive Tract

The urogenital system is formed mainly from mesodermal tissue that in early embryonic life forms the nephric and genital regions. In the cranial portion of the nephric region, segmental tubules initially form the **pronephros** each with a pronephric duct that runs to the primitive cloaca. Later other segmental tubules form caudal to the pronephros and unite with the pronephric ducts to form another temporary excretory organ, the **mesonephros and mesonephric ducts or Wolffian body and ducts**, and the pronephros degenerates. Later a third and more permanent excretory organ forms more caudally from an outgrowth of the mesonephric duct to become the **metanephros or true kidney** with its ureter and bladder. The mesonephros then degenerates but its duct system is utilized in the male to transport spermatozoa from the testes to the pelvic urethra. The development of the paramesonephric (Mullerian) duct has been described in the section on the embryology of the female genital tract. Remnants of the paramesonephric or mesonephric ducts may persist in the adult male as the **appendix testis** and the **uterus masculinus**. In the fetus most of the urine from the fetal kidneys passes into the bladder and through the urachus into the allantoic cavity.

The **testes** form initially as undifferentiated gonads late

in the embryonic period in the genital region or gonadal or genital ridge between the dorsal mesentery and the mesonephros. Although the sex of the embryo is determined at the time of fertilization, sexual differentiation does not occur until the early fetal period after the primordial germ cells have migrated, about day 26 of gestation in the bovine fetus,⁶ to the gonadal ridge from the wall of the yolk sac in the region of the hind gut and structural changes occur in the gonad. Testis cords, rete testis cords and the tunica albuginea form early in the fetal period. Primary medullary cords are characteristic of the early male gonad. These testis cords of primitive germ cells and supporting Sertoli cells remain solid until just before puberty when the seminiferous tubules are formed and join the rete testis by means of the tubuli recti. The rete testis in turn enters the efferent tubules, epididymis and ductus deferens that are formed from the mesonephric tubules and duct. Certain tubules of the mesonephros that do not form the duct system of the testis may remain as small remnants called the **ductuli aberrantes**, blind-ending ductules,⁷ **appendix testis** near the head and the **paradidymis** near the body or tail of the epididymis. During the middle trimester of gestation interstitial cells are numerous especially in the equine fetus.

In the very early fetal period the external genitalia in the cloacal region are also in the indifferent stage characterized by a **genital tubercle** which elongates to form the phallus or penis with two genital folds that form the urethra and the two genital swellings that form the scrotum. Development of the external genitalia in males is hormonally controlled by androgens presumably from the fetal gonad. (See Table 2.)

During fetal development, the testis covered by the visceral peritoneum moves caudally from its location near the caudal pole of the kidney guided by the **gubernaculum testis**.^{1a,4,6,12} At the same time the **vaginal process** forms as an invagination the body cavity with its parietal peritoneum into the genital swelling and gubernaculum. Only in the bitch is this female vaginal process still visible in the adult animal. As the testis approaches the internal vaginal ring of the inguinal canal, the caudal part of the gubernaculum increases enormously in size dilating the inguinal canal and scrotum. It may be mistaken in some fetuses for the descended testis. As the enlarged jelly-like mass of the gubernaculum decreases in size and shrinks, the testis sinks through the inguinal canal and into the scrotum where the gubernaculum forms the proper ligament of the testis and the ligament of the tail of the epididymis. It is possible that the scrotal fascia and the external cremaster muscle are also derivatives of the gubernaculum.³ Thus the testis always remains outside

the peritoneal cavity but the vaginal cavity formed between the tunica vaginalis parietalis, the parietal layer of peritoneum, and the tunica vaginalis visceralis, the visceral layer, is continuous with the abdominal cavity throughout life. If the internal inguinal ring is large, an inguinal or scrotal hernia may develop in this cavity.

Testicular descent and enlargement of the gubernaculum is probably hormonally controlled by androgens from the testes. Failure of normal testicular descent appears in most cases to be genetic in nature and results in cryptorchidism seen most commonly in boars, stallions and dogs and least commonly in bulls, rams, bucks and toms. An abnormal development of the gubernaculum and other factors^{1a} could account for the cryptorchid condition.¹² Testicular descent into the scrotum occurs in the domestic animals during the following periods: horse, 10 to 11 months of gestation; cattle, 3-1/2 to 4 months of gestation; sheep, 2-2/3 months of gestation; pig, 3 months of gestation, and dog, about 7 to 21 days after birth.^{2,8}

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Physiology of Male Reproduction

Hormones—In the developing male embryo soon after the primordial germ cells have migrated to the gonads,

differentiation into a testis with recognizable medullar¹ cords occurs sooner than in the female in which cortical cords develop more slowly. The primitive testis apparently secretes or produces androgens that are responsible for the development of the mesonephric duct system and the formation of male external genitalia. The testis also produces a "Mullerian" inhibiting substance" that suppresses the development of the paramesonephric ducts.^{3,8} A lack of this substance or "androgen" which occurs when the testes are removed experimentally early in the fetal period results in differentiation into female genital organs. Excessive and prolonged doses of androgens given to animals in early pregnancy may cause a degree of masculinization of the external genital organs of the female fetuses.

Prior to the onset of puberty, releasing substances, GnRH, secreted by the sex centers in the hypothalamus, pass through the hypophyseal portal system to the anterior pituitary gland to cause the release of the protein, water-soluble gonadotropic hormones from the basophilic delta cells. The gonadotropic hormones are the same as in the female and consist of two closely associated fractions FSH and LH or ICSH (interstitial cell-stimulating hormone). FSH has been considered responsible for spermatogenesis from the initial division of spermatogonia through the formation of the secondary spermatocytes. Thereafter testosterone is thought responsible for sperm cell development. These hormones in the male animal are released in episodic surges or bursts or pulses lasting several minutes to several hours. This results in wide hourly variations in plasma testosterone levels.¹⁷ Following the injection of HCG the level of plasma androgens in stallions will double or triple within several hours. About 4 to 8 episodic bursts or releases of testosterone occur daily in the stallion.² Hormones may not be required for the progression from a spermatogonia to the late stages of primary spermatocytes.¹⁹ Testosterone is required for the reduction division of primary spermatocytes and possible early spermatid formation. ICSH (LH) stimulates the growth of the interstitial or Leydig cells located between the seminiferous tubules in the testes and the secretion of testosterone and other androgens from these cells. All gonadotropins are prepared from biologic sources as they are complex high-molecular weight proteins. Chorionic gonadotropin (HCG) from the urine of women in early pregnancy and sheep pituitary and purified pituitary products from other animals with a high LH (ICSH) content are commercially available. Equine gonadotropin (PMSG or ECG) either from the endometrial cups or equine or other purified animal pituitary products high in FSH activity are also available. Levels of gonadotropic hormone, especially FSH, are high in

castrated mature animals and postmenopausal women. (See Figure 162.) Gonadectomy or castration is widely used in domestic animals to eliminate undesirable aggressive male sexual behavior and undesirable carass qualities including boar and buck odor.⁸

In animals having a breeding season regulated by either increasing or decreasing daylight such as the horse, sheep, goat and possibly the cat, the levels of plasma ICSH (LH) and testosterone are highest in males during the breeding season and lowest during the nonbreeding season.¹⁶ Most males continue to be able to copulate and fertilize but at a somewhat lower efficiency during the "nonbreeding" season.^{2,12b,14}

Hypophysectomy is followed by involution of the seminiferous epithelium and a lack of libido; injections of FSH and ICSH (LH) can restore spermatogenesis, libido and ejaculation of normal motile spermatozoa.¹⁰ The amounts of FSH and ICSH produced and secreted are controlled by feedback mechanisms whereby high levels of testosterone and other gonadal steroids and "inhibin," peptides, from the seminiferous epithelium, probably the Sertoli cells,^{17,22} act on the hypothalamus and/or anterior

pituitary gland to decrease the production of gonadotropic hormones, especially FSH. High continuous levels of testosterone or other gonadal or anabolic steroids such as progesterone, progestins, or estrogen, maintained by either parenteral injection, feeding, or from steroid-producing tumors of the testes or adrenal gland will cause degeneration and atrophy of the seminiferous epithelium and the interstitial cells. This process can be reversed by withdrawal of the exogenous source of steroids, resulting in the "rebound phenomena."

In the stallion total androgen and estrogen plasma concentrations were 2.0 to 2.5 ng/ml. and 30 to 40 pg/ml., respectively.² An injection of 1500 IU of HCG more than doubled the androgen concentration within two hours but had no effect on the estrogen concentration in the stallion and dog. The average testosterone level in canine blood plasma was 1 to 4 ng/ml.^{9b} The high level of estrogens found normally in stallion urine is due to estrogen production by the sustentacular, supporting or Sertoli cells of the seminiferous tubules of the testis. Sertoli cell tumors of the canine testis are not uncommon and produce high estrogen levels with signs of feminization and tes-

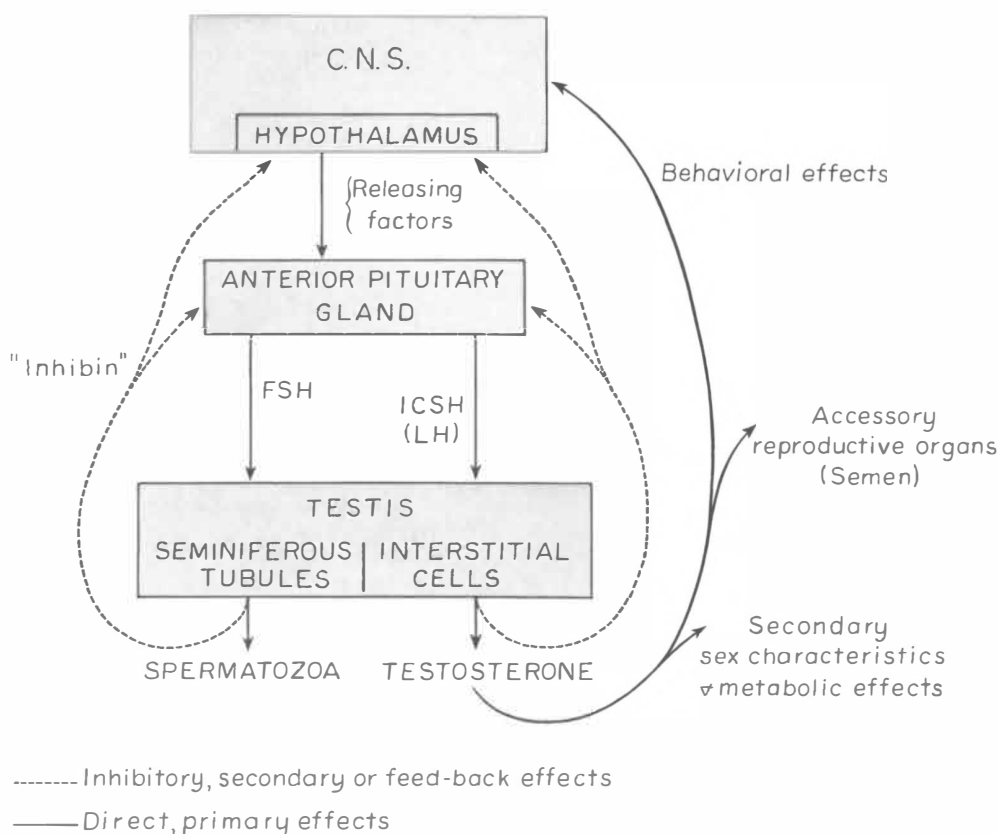


Figure 162. Diagram of the Neuroendocrine Control of Reproduction in Male Animals.

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 ticular atrophy. Sertoli cells have a number of important functions including the secretion of fluid into the seminiferous tubules. Rete testis fluid and seminiferous tubule fluid differ in composition from blood plasma and testicular lymph indicating the presence of a blood-testis barrier.¹⁷

Testosterone, a steroid hormone, is soluble in oil or alcohol but not in water. In the interstitial cells the biosynthesis of testosterone is as follows: acetate → cholesterol → progesterone → androstenedione → testosterone. Testosterone is the major androgen elaborated by the testis in the bull, dog and human. In the bull testosterone is 16 times more active than androstenedione. The latter is the major androgen in the stallion testis.^{15b} These authors reported an average androgen titer of 3.0 micrograms per ml. in the peripheral plasma of 3 to 4-year-old bulls. In 3 of 4 bulls injected daily with large doses of HCG a marked increase in the androgen level was produced. Based on studies of prostatic fluid, 2.5 mg per kg. of body weight daily of testosterone was needed to maintain prostatic function in male canine castrates.^{15a} Androgens are excreted in the urine as androsterones.

Testosterone or androgens from the testis are necessary for: (1) the sexual differentiation of the external male genitalia, and the descent of the testis into the scrotum in fetuses or neonates;^{2,3,17} (2) the keratinization of the preputial epithelium, the separation of the glans penis from the prepuce; (3) the growth and maintenance of the accessory genital glands so they can contribute their secretions to the semen at the time of ejaculation; (4) sexual desire or libido and the ability for normal erection and copulation; (5) secondary sex characteristics of hair and horn growth, male attitudes, timbre of the voice, increased bone thickness, increased muscle tissue with a different distribution of fat from the female due to protein anabolic effects; (6) the maintenance of secretory and absorptive activities and structures of the efferent ducts, epididymis and ducti deferentes including the ampullae, and (7) spermiogenesis or development and maturation of the spermatids and spermatozoa in the testicular and mesonephric ducts are largely maintained by testosterone produced by the interstitial cells which in turn are stimulated by ICSH. High levels of testosterone are present in the lymph and fluid around the seminiferous tubules of the testis. Testosterone enables diakinesis and meiosis to occur.¹⁷ Testosterone can restore sexual desire and copulatory ability when injected into the castrated male animal. Estradiol when administered to steers was highly potent in stimulating most male sexual behavioral characteristics. Testosterone may exert part of its effect on steers and normal males by conversion to estradiol in the brain or hypothalamus.^{5b}

The sheath or prepuce is a modified skin membrane and not a true mucous membrane. It is rich in glands producing sebum and smegma. The preputial glands, which are under the influence of testosterone, are located in the dorsal lateral region of the preputial orifice of boars. They are modified sebaceous glands that are responsible, together with the preputial diverticulum, that fills with smegma, urine and semen from masturbation, for the typical boar odor. These preputial glands that secrete a muscone type of material, a combination of 16 androstenes,⁹ may be surgically removed along with the preputial diverticulum to eliminate the characteristic odor of boar tissues. An immunization attempt against the boar taint steroid, androstenone A, was unsuccessful.^{18a} The highly odoriferous musk-like odor characteristic of adult intact male goats may be due in part to 6-trans nonenal¹⁸ but further studies are necessary in this animal. In goats these glands are located in the caudo-medial skin at the base of the horn. By removing this area of skin, about 24 × 14 × 5.5 mm., at the time of dehorning prepubertal male goats, the odor characteristic of mature male goats is eliminated.^{6b,7,21} These odoriferous chemical compounds are called pheromones that elicit either or both sex attraction or mating behavior through their action on the brain and hypothalamus.¹²

Castration, if performed before puberty, prevents the development and function of those organs and activities requiring testosterone and if performed after puberty results in the atrophy of organs and of activities that are testosterone dependent. There are no interstitial cells in the epididymis so the early belief and practice of "cutting a horse proud" by leaving a portion of the epididymis at the time of castration is fallacious.^{4a,b} There is no antagonism between estrogens and androgens per se. Their apparent antagonism is due to their similar effects on the hypothalamus and the anterior pituitary gland in preventing the release of the gonadotropic hormones. Marked abnormal antler growth in deer with severe hypogonadism was reported.²¹ In the bull interstitial cells were active by 3.5 months of age and the androgen content of the testis increased through 5 years of age and from then on tended to decrease.¹ This decrease in plasma androgen concentration is reported in other animals at older ages.¹⁷ Undernutrition also reduces testosterone levels by reducing gonadotropin production or release.¹⁷

Occasionally male, or female, reproductive steroid hormones are produced by adrenal cells or tumors. Presently all commercial veterinary sources of androgens are synthesized from cholesterol-like compounds and are sold in solution in oil or alcohol ("Repositol"), in suspension in aqueous preparations, or in pellets for implantation. Testosterone may be administered orally especially to dogs

and cats because of their simple stomachs.

Oxytocin administered intramuscularly prior to ejaculation in a limited number of bulls has resulted in a larger volume and greater numbers of spermatozoa in the ejaculate. Contractile mechanisms involved in sperm transport in the male are in part regulated by oxytocin. (See erection and ejaculation.)

Although they are essential for normal body function other pituitary hormones such as ACTH, somatotrophic hormone, prolactin, thyrotrophic hormone, and oxytocin and vasopressin, as well as thyroxine from the thyroid gland, the glucocorticoids and adrenaline from the adrenal gland and others have only moderate secondary effects of limited importance on reproduction in the male domestic animal.

Puberty—The onset of puberty in male domestic animals occurs at approximately the same time after birth as puberty in females of the same species. About 4 months of age GnRH from the hypothalamus causes the episodic release of gonadotropic hormones, LH and FSH, from the anterior pituitary gland resulting in the secretion of androgenic hormones from the gonads that cause growth of the genital organs and secondary sex characteristics.^{17,13,15,17} Injections of gonadotropic hormones into prepuberal animals results in precocious sexual maturity. In the male the onset of puberty is characterized by secondary sex signs, sexual desire, ability to copulate and the presence of viable spermatozoa in the ejaculate. The onset of puberty is a gradual process and is variable in time since it may be influenced within a species by the plane of nutrition, breed of animal (**Bos indicus** bulls mature slowly than **Bos taurus** bulls), cross-breeding, methods of management, presence of chronic disease processes, and individual differences.^{2,6}

The development of puberty in bulls has been carefully studied.^{1,11,13-17} Primary spermatocytes appear in the seminiferous tubules by 4 to 6 months of age, spermatids by 6 to 7 months, and spermatozoa by 7 to 9 months of age in bulls. Seminal secretion from the accessory glands appears by 5 to 6 months. Separation of the penis from the sheath in bulls proceeds caudally beginning at 1 month and ending with complete separation by 8 months of age. The period from 6 to 10 months of age in bulls is characterized by the accelerated growth rate of the genital system, increases in GnRH and in plasma LH, external manifestations of puberty and the rapid onset of spermatogenesis. Puberty was reached at 10 months, 40 weeks, in well-fed, healthy Swedish Red and White bulls and by 12 months, 48 weeks, when fed on a lower plane of nutrition. However others⁷ have reported that fertile semen with conception has been produced by well-reared bulls at 6 months of age. Puberty probably commences

at 2 months and is qualitatively completed by 10 months of age in Holstein bulls.¹⁸

The onset of sexual behavior in a young male is significantly hastened by rearing with other males or females and is retarded by rearing in isolation.¹⁶ The size of the testis in prepubertal bulls increases rapidly between 4 and 8 months of age and then growth of the testes is at a slower rate and is correlated with the body weight. During the pubertal period it may be difficult, without repeated examinations over a number of months to differentiate between delayed testicular development due to poor nutrition and management or testicular hypoplasia caused by genetic or congenital influences.¹⁶

The penis of newborn ruminants and swine is without a sigmoid flexure and is adhered to the prepuce. Penile growth due to androgens between 3 and 8 months of age results in the development of a sigmoid flexure and its separation from the prepuce. A scrotal circumference of 28 cm. is indicative of puberty in bulls.^{13,14,15}

The attainment of puberty does not signify full reproductive capacity. Highly significant increases in ejaculate volume, output of motile spermatozoa and concentration of spermatozoa occur in bulls for 6 to 9 months after the onset of puberty.^{2,3,8} Puberty in bulls was defined as the age at which the first ejaculate containing at least 50×10^6 spermatozoa with 10% motility was obtained.¹⁵ Within 4 months after puberty the percentage of normal acrosomes had not yet reached mature levels.¹⁴ A marked reduction between 9 and 12 months in the number of proximal protoplasmic droplets on bovine spermatozoa was noted.² The same reduction in protoplasmic droplets and abnormal spermatozoa in ejaculated boar semen occurred between 150 and 200 days of age.¹² The rapid growth of the testis and epididymis from 4 to 8 months of age in the boar was described.^{20,21} Detachment of the sheath from the penis occurred at 4 to 6 months and sexual maturity in the boar was reached at 7 to 8 months of age. It was noted that 16 to 17-month-old stallions produced only 16.4 ml. of gel-free sperm per ejaculate with 22 percent progressive motility and 48 percent abnormal sperm cells.¹⁰ Because of the above indications of a lack of maturity after the onset of puberty and because of individual differences in libido, spermatozoan reserves, and the ability to produce large numbers of normal spermatozoa, immature male animals should be used sparingly for breeding purposes for one-half to one year or more after reaching puberty. Bulls that mature early with large testicles generally produce daughters that also mature early and may be more fertile.⁹ Scrotal size in young bulls was not highly correlated with sexual behavior or libido.¹³

The time of puberty in male animals is:

- Stallions—18 months (range 12 to 24 months)
 Bulls—9 to 12 months (range 6 to 18 months)
 Rams and Bucks—7 to 8 months (range 4 to 12 months)
 Boars—5 to 7 months (range 4 to 8 months)
 Dogs—7 to 10 months (range 5 to 12 months)^{11b}
 Toms—8 to 10 months (range 6 to 15 months)

The Scrotum and Heat Regulation of the Testes—

The testicles in all domestic animals are normally located in the scrotum. In certain wild species of rodents the testes are retained in the abdominal cavity except during the breeding season when they descend into the scrotum. The whale, elephant, rhinoceros and seal have no scrotum and the testes are intra-abdominal. In the domestic animals the scrotum performs a vital temperature-regulating function for the testes. If the testes are maintained at body temperature, as occurs in bilateral cryptorchidism, spermatogenesis does not occur. High, prolonged fevers, insulation of the scrotum or prolonged exposure to high atmospheric temperature and humidity can also seriously impair spermatogenesis. However, testosterone production by the interstitial cells or Leydig cells is not affected by temperature.

The dartos muscle, by contracting in cold weather to hold the testes against the body and relaxing in warm weather is the principal thermoregulator of the testis.² The external cremaster muscle, by raising the testis, may also play a role. In the dog, bull, boar and stallion the scrotal skin is thinner and less well covered with hair which together with increased numbers of sweat glands further assists in cooling the testes.¹⁷

Scrotal temperature in three dairy bulls varied from 93.2° F (34.1° C) to 100.4° F (37.9° C) while rectal temperature varied from 100.4° F (37.9° C) to 102.2° F (38.9° C) during the same 8-hour period.¹ Scrotal temperature can rise rapidly when bulls recline. Fluctuations of 18° F (10° C) in environmental temperature had little effect on scrotal temperature. The testicular temperature of the ram may vary from about 85° F (28° C) to about 104° F (40° C). In animals with well-developed scrotums the testicular temperature is usually 2 to 7° C below body temperature.¹²

In rams blood in the coiled internal spermatic artery winding through the pampiniform plexus of spermatic veins cools 9.4° F (5.2° C) when the testicular temperature is about 93.2° F (34° C).³ The arrangement of the spermatic artery and vein in the region of the pampiniform plexus provides an efficient heat exchange mechanism that, although it is not regulatory, rapidly transfers any benefit of scrotal thermoregulation to all parts of the testis. In this regard in the bull the extensive network of superficial veins in the tunica albuginea plays an im-

portant role in lowering the temperature of the venous blood before it passes through the tortuous spermatic vein.

The Testes, Spermatogenesis and Spermiogenesis—The testes perform a dual function in producing testosterone from the interstitial cells, and spermatozoa and "inhibin" from the seminiferous tubules. The mature male domestic animal is capable of fertile copulation at any time. However, in certain wild animals such as deer, camels and elephants there is a definite seasonal period of sexual excitement or "rut" and spermatogenesis occurs only during this period. In some domestic animals, such as the ram and stallion, there may be seasonal variations in libido and in spermatogenesis and semen quality due to environmental nutritional, length of daylight or other factors.

Spermatogenesis is a highly synchronized process whereby spermatozoa are formed from the precursor diploid cells, type A spermatogonia.¹⁷ **Spermatogenesis** includes both **spermatocytogenesis** (spermiocytogenesis) or formation of primary and secondary spermatocytes from type A spermatogonia and **spermiogenesis** or the formation of mature fertile spermatozoa from the immature spermatids. Spermatocytogenesis is under the regulation of FSH from the anterior pituitary gland and conditions favorable for spermiogenesis are under the control of LH and testosterone. Under normal conditions spermatogenesis is a very orderly continuous process. In any single small area of the seminiferous epithelium various stages of the well-organized extremely regularly occurring cycle of the seminiferous epithelium may be observed.

The duration of spermatogenesis is comprised of 4 cycles (4.68 cycles if spermatogenesis is started with a dormant type A spermatogonia) of the seminiferous epithelium starting with type A spermatogonia. At each cycle of the seminiferous epithelium the spermatogonia renew themselves by producing new stem cells and cells that will produce spermatocytes. Each cycle length in the bull and dog^{9b} is 13.5 days, in the boar 8.6 days and in the ram about 12.2 days. In the boar, bull and ram and other male animals a succession of 8 highly characteristic cellular associations or stages occur in each cycle which takes place in the form of a spiral along a portion of the seminiferous tubule as well as at one transverse area. In each stage there are several distinct groups of cells present on cross-section of the seminiferous tubule. At stage 8, for example, nearly mature spermatozoa line the lumen of the tubule. Spermatids at a certain stage in development, or a generation of germ cells, are always associated with the same types or other generations of spermatogonia and spermatocytes. The distance between two similar cellular associations or stages in the seminiferous tubule is called a spermatogenic wave.^{8,9,16} A

second classification of 14 cell associations forming the spermatogenic cycle has been described.^{8,17} (See Table 22.) Any agent that damages spermatogonia could lead to permanent damage of the testis; but if only differentiating cells are damaged, repair is possible.

Spermiogenesis begins as soon as the spermatid is formed. At this stage the spermatid has a spherical nucleus surrounded by cytoplasm containing many mitochondria in which a Golgi complex or zone soon forms. The acrosome and head cap of the spermatozoon arise from the Golgi complex. The cytoplasm and centrioles move to the opposite side of the nucleus. The centrioles give rise to the flagellum or axial filament and later the body and tail of the spermatozoon. The mitochondria later become arranged like a collar around the upper region of the flagellum as the mitochondrial helix forming the middle piece. At the end of spermiogenesis when the spermatozoa are in the head of the epididymis, unused cytoplasm and Golgi material, now called the protoplasmic or cytoplasmic droplet, is located in the neck region of the sperm cell in the testis, and is cast off as the spermatozoa pass through the epididymis.²

During part of its transformation to a spermatozoon the spermatid is closely associated with "nurse" or Sertoli cells in the seminiferous tubules. After it leaves the Sertoli cell and is "free-living" in the lumen of the seminiferous tubules it is moved into the rete testis and efferent tubules by a large volume of secreted fluid from the Sertoli cells and cells lining the rete and efferent tubules.¹⁷ There is little evidence of any contractile tissue and no cilia in the seminiferous tubules, straight tubules or rete testis. Spermatozoa do not develop any significant degree of motility until ejaculation. The testicular capsule apparently contains smooth muscle that contracts and relaxes and this alternate activity exerts a pumping action on the seminiferous tubules forcing the nonmotile sperm cells and "plasma" out of the testis and into the epididymis.

Normal bulls and stallions produce 12 to 17 million and rams 12 million spermatozoa per gram of testicular tissue daily.^{2,14,18,9,16} Boar produce 25 to 30 million sperm cells per gram of testis daily because of the shorter duration of spermatogenesis and the larger number of spermatozoa produced from one type A spermatogonium.¹⁰

Table 22. Outline of Spermatogenesis in the Bull, Boar and Ram

		Chromosome Complement	No. of** cells	Time in Days*		
				Bull	Boar	Ram
Type A Spermatogonia (dormant)		2N (diploid)	1			
Type A Spermatogonia		2N	2			
Intermediate Type Spermatogonia		2N	4			
Type B Spermatogonia		2N	8			
Primary (Preleptotene) Spermatocytes (active DNA synthesis)		4N (tetraploid)	16			
Leptotene stage						
Zygotene stage	Meiotic					
Pachytene stage	Prophase I (long, 16 days in ram)					
Diplotene stage						
Diakinesis						
Metaphase I					25-26	
Anaphase I	1st Meiotic (maturation)			40-42		
Telophase I	Division					36-37
Secondary Spermatocytes		2N	32			
Diakinesis	Meiotic Prophase II (very short, hours)					
Metaphase II						
Anaphase II	2nd Meiotic (maturation)					
Telophase II	Division					
Spermatids		1N (haploid)	64			
Spermatozoa	Spermiogenesis (long, 15 days, ram)	1N	64			

*It takes approximately 10 days in the bull and 13-15 days in the ram and boar for spermatozoa to traverse the epididymis. Thus from type A spermatogonium to ejaculated spermatozoa is about 60 to 70 days in the ram and bull and 50 to 60 days in the boar, stallion and dog.

**Theoretically in the bull and ram 16 primary spermatocytes and 64 spermatozoa develop from one type A spermatogonium; boars and rats have 24 primary spermatocytes and 96 spermatozoa from one spermatogonium. However a certain loss in cells, about 25%, is experienced during meiosis and is characterized by the presence of pycnotic nuclei.

Thus daily sperm cell production for a bull with testes weighing 400 gms each, a stallion with testes weighing 85 gms. each, a ram with testes weighing 250 gms. each, and a boar with testes weighing 300 gms. each would be 12 billion, 6 billion, 7 billion and 15 billion spermatozoa, respectively. About 70,000 spermatozoa are produced every second during the breeding season by the testes of an adult stallion.² Sperm numbers in the testis are highly correlated with testis weight, testis diameter, testis tone or consistency, and scrotal circumference.^{3,5} Testicular growth continues through puberty until complete sexual maturity occurs, which in the bull is about 4 years of age. Beef breeds, particularly **Bos indicus**, mature more slowly than the dairy breeds. Scrotal circumference in normal bulls is closely correlated with spermatozoa production since 70 to 90 percent of testicular weight is comprised of the seminiferous tubules. In most beef bulls average scrotal circumference increases from 14 months, to 26 months to 36 months of age from 33 cm. to 35 cm. to 36 cm., respectively. While in Brahman bulls the corresponding age-related average circumferences are 22 cm. to 32 cm. to 37 cm. and in Holstein bulls 32 cm. to 39 cm. to 42 cm., respectively.^{3,5} Measurements are made with scrotal circumference tapes.*

Other factors that influence bovine testicular size besides age and breed is body condition, body weight, season (heat stress)¹⁷ testicular pathology. Testicular size is highly heritable.⁵ Bulls of breeding age should have a scrotal circumference measurement of 32 to 34 cm. or more to be classified as a "satisfactory potential breeder."^{5,6} The testes of other animals also increase in size from puberty to maturity. In the stallion under 12 months of age the total testes weight is 53 gms., at 24 months it is 209 gms., at 36 months, 232 gms., and at 4 to 10 years, 317 gms.² Testicular size in stallions may be measured by calipers.¹⁴ As in other animals total scrotal width is closely correlated to testicular weight and production of spermatozoa. The average scrotal width of normal stallions is 105 mm., range 80 to 140 mm. Equine testicular size decreases 10 to 15 percent in the nonbreeding winter season and as stallions age the testes increase in size from 90 mm. scrotal width in 2 year old to 108 mm. in 15 year old horses. Individual testis width in Standardbred stallions averaged 4.6 to 6.3 cm. with the right testis slightly larger than the left in all ages. A 9 to 18 percent reduction in size of testes of like aged horses occurred in working, stressed, or hormonally treated stallions at racetracks compared to breeding farm stallions.¹⁹ During the nonbreeding season in sheep scrotal

circumference in rams was 15 percent less than during the breeding season.¹⁴

Scrotal circumference in rams varies with the weight and age of the ram. Scrotal circumference of normal, well grown rams was 26, 33, 34, 36 cm. for rams weighing 100, 150, 200, 250 and 300 pounds, respectively, with a range of 20 to 43 cm.^{16b} Heritability estimates for scrotal circumference were high and for testis consistency medium. These traits should be emphasized in bull evaluations.^{5b}

Four months after unilateral castration in the ram and prepubertal bull the weight of the remaining testis increased by about 76 percent and sperm cell production was nearly double that of a normal testis.^{1b,18} As in rabbits and dogs after hemicastration the diameter of the seminiferous tubules increased greatly to produce a compensatory hypertrophy of the single testis. Further study of this interesting observation is needed in these and other species.

The Morphology of Spermatozoa—In recent years electron microscopy has done much to elucidate the fine structure of spermatozoa. Although the size and shape of spermatozoa differ between the domestic species of animals the basic morphological structure is similar. The head length and width is about 8 to 10 microns by 4 to 4.5 microns in bull, ram and boar spermatozoa and smaller, 5 to 7 microns in length and 2.7 to 4.0 microns in width, in stallion, dog and cat spermatozoa. The head thickness is about 0.5 to 1.5 microns or less in all species. The spermatozoan body or middle piece is about one and one-half to two times as long as the head, 10 to 15 microns, and about 1.0 micron in diameter in all species. The tails of spermatozoa are 35 to 45 microns long and 0.4 to 0.8 microns in diameter. The total length of spermatozoa of domestic animals is thus about 50 to 70 microns or 1/300 of an inch.^{8,17,14}

The head of the spermatozoon is elongated and ovoid in shape, broad and flat in one plane and narrow in the other with the thickest portion at the base and tapering to a fairly thin apex. The head is entirely filled with a nearly homogenous nuclear material containing the genetic material, DNA or deoxyribonucleic acid, surrounded by the nuclear membranes. (See Figure 163.) DNA is the amazingly concentrated coded genetic material. Each spermatozoon contains about 2.5 billion bits of information necessary to form a fetus yet it takes 300 billion spermatozoa to make 1 gram of DNA.⁶ The anterior part of the nuclear membrane or the inner membrane of the acrosome forms the body of the acrosome. The anterior 60 percent of the nucleus and its modified membrane, is covered by the acrosome cap or head cap which is a double-walled pouch-like structure about 0.1

*Lane Manufacturing Co., 5560 E. Pacific Place, Denver, Colo. 80222.

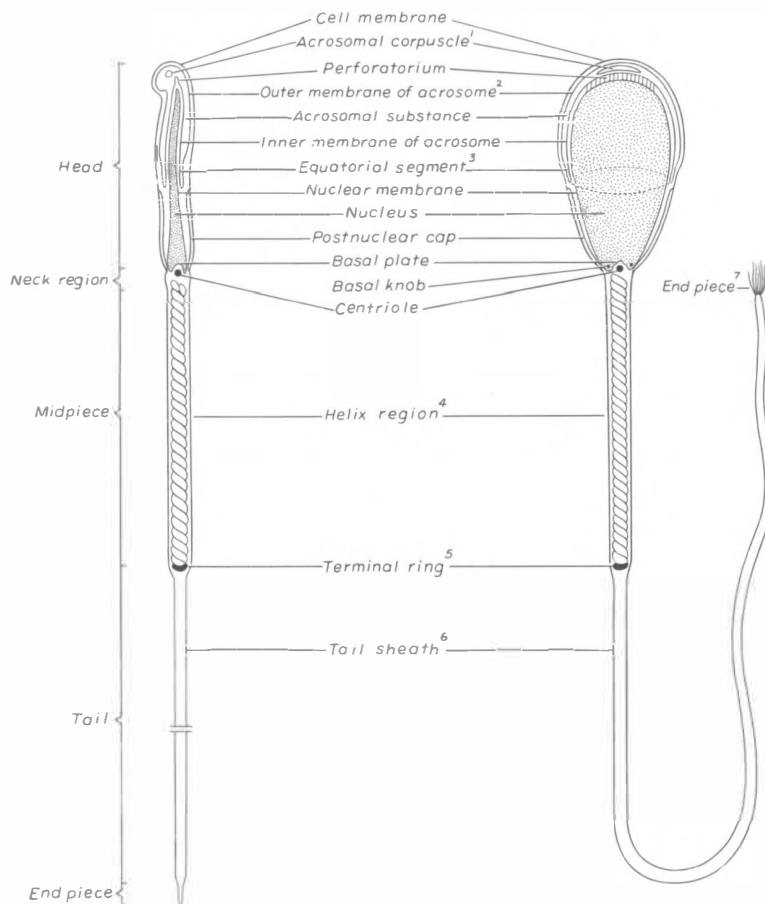


Figure 163. Diagram of the Ultrastructure of the Sperm Cell. 17, 4, 10 Synonyms: 1. Acrosomal Vacuole or Apical Body 2. Galea Capitis or Sperm Cap 3. Equatorial zone 4. Mitochondrial Helix 5. Jensen's Ring 6. Cytoplasmic or Fibrillar Sheath 7. Terminal Filament.

micron thick enclosing the acrosomal substance and the denser acrosomal corpuscle, body, or vacuole.^{17,4,10} The equatorial zone or segment is the posterior part of the acrosome or head cap around the middle portion of the sperm head corresponding to the area where the acrosomal substance is most scanty. The posterior 40 percent of the nucleus and nuclear membranes from the equatorial zone to the base of the cell are covered by the postnuclear cap or nuclear sheath. The differences between the acrosome cap and postnuclear cap explain the differences in affinity for stains observed in these two regions. The cell membrane composed of several layers completely encloses the head, body, and tail of the spermatozoon. The membrane is closely applied to the cell at the anterior portion of the acrosome cap, the postnuclear cap, and at Jensen's ring. The outer membrane of the acrosome cap, is identical with the galea capitis, described in the earlier literature, that is detached either

spontaneously in the tail of the epididymis by long, sexual abstinence, artificially in vitro, or during fertilization, probably as a step in sperm capacitation. Detachment occurs by rupture of the cell membrane and the outer membrane of the acrosome cap in the equatorial zone which exposes enzymes such as hyaluronidase in the acrosome that are necessary for penetration of the spermatozoa into the ovum.^{17,7} It was recommended that earlier term "perforatorium" be dropped as the function ascribed to it is performed by the acrosomal body.⁷ The detached outer membranes of the acrosome may break into two halves, or remain joined and appear as "bathing-cap" shaped structures in stained or India ink preparations of semen.

The neck, centriolar region or implantation zone, about 1.5 microns long, consists of the two centrioles and their surrounding radices or implantation plates.^{8,17} The mitochondrial sheath originating in the basal knobs or gran-

ules of the head form two counter-clockwise spiral structures, the mitochondrial helices, that continue down the body or midpiece to the terminal or Jensen's ring. The radices change into the fibrillar bundle at the posterior portion of the neck region. Most authors consider the neck region as part of the body or middle piece. The mitochondrial sheath is about 0.1 micron in thickness and surrounds the fibrils, 9 coarse or peripheral and 11 fine or central. These latter structures resemble cilia. The helix region, midpiece, middle piece, or body supplies energy for the sperm cell by metabolic processes occurring in the mitochondrial helix. The tail region, the longest part of the sperm cell originates at the terminal ring of the body and extends to the endpiece. In the tail region, the fibrils are surrounded by the fibrillar coil sheath or tail sheath consisting of pair of spiral coils with each of the coils making more than 400 spirals. The endpiece or terminal portion of the tail is about 3 to 4 microns in length and consists of the terminal portion of the fibrils covered by the cell membrane but the fibrillar coil sheath of the tail is absent.¹⁰ The wave-like or whip-like action of the tail originates in the neck region of the body and generates contractile force as it proceeds distally. Helical oscillations of the tail of the spermatozoon are very rapid and provide the force necessary for sperm cell motility which under optimum conditions of temperature, and medium is about 100 microns per second, range 10 to 352, in bull spermatozoa,^{3,9,11,12,13} or about 4.23 mm. per minute.² The motility rates for equine, ovine and human spermatozoa were 80 to 100, 200 to 250 and 30 to 75 microns per second, respectively.

Spermatozoan Transport, Maturation and Storage and Accessory Gland Secretion—Spermatozoa are carried in a large amount of fluid secreted by the seminiferous epithelium into the rete testis and the tortuous efferent ducts (ductuli efferentes) usually about 13 to 15 in number, located adjacent to the head of the epididymis and opening into the epididymal duct.^{8,17} These structures since they arise from the mesonephros have kidney-like functions in respect to absorptive and secretory activities. As mentioned previously contractions of the testicular capsule probably aids in forcing semen from the testes into the efferent ducts. Nearly all of the fluid, 200 ml. daily in the bull, entering the efferent ducts and head of the epididymis in the bull, as well as the boar, was reabsorbed there.^{17,10} About 30 ml. of fluid passes daily from the rete testis into the efferent tubules of the ram.³² The sperm cell concentration in this fluid was 100 million per ml. Ligation of the efferent ducts and possibly the head of the epididymis caused an accumulation of fluid or edema in the testes followed by atrophy while no accumulation occurred if the ligature was placed around

the more distal portions of the epididymis.^{17,28} Both secretory cells and cells with cilia beating toward the epididymis are found in the efferent ducts. The ciliated borders of these cells in the bull may become detached and excreted with the semen at the rate of one "medusa head" per 10,000 spermatozoa or about 500,000 in the average ejaculate.⁹ Smooth muscle activity as well as ciliary activity help transport sperm through the efferent ducts.

In the epididymis peristaltic activity of smooth muscle is largely responsible for sperm transport. Microvilli are present in epididymal cells but they are nonmotile. The contractile mechanisms involved in sperm transport in the male are partly regulated by oxytocin. The epididymal epithelium has absorptive and secretory functions producing variations in the sodium, potassium, calcium, chlorine and phosphorus ion concentrations and in the concentrations of proteins, enzymes and glycerylphosphorylcholine in the luminal contents in different portions of the epididymis.¹⁴ The composition of epididymal plasma is closely related to testicular function, the passage of sperm cells and the hormonal and physical testicular environment. Plasma volume in bulls was doubled by secretions in the caput and halved by absorption in the cauda; while in boars the epididymal content underwent continuous dilution from the caput to the cauda epididymis. The time required in the domestic animals for spermatozoan transport through the head, body and tail of the epididymis is about 7 to 15 days. Frequent ejaculations hasten the passage of spermatozoa through the tail of the epididymis.²

Although physiologic mechanisms of the epididymis are largely under the hormonal control of testosterone they are not well understood. The sperm cell undergoes maturation and other changes including the ability to become motile and fertilize an ovum,^{2,17} in its passage through the epididymis. An example of this maturational process is the passage of the cytoplasmic droplet from the neck region, down the middle piece and tail from which it is lost before ejaculation. This is most commonly described in ungulates. Proximal protoplasmic droplets were present on 44% of the spermatozoa in the caput and only 2% in the cauda epididymis of bulls.⁴ The percent of proximal protoplasmic droplets in the caput of swine is higher. Spermatozoa removed from the tail of the epididymis were 2 to 10 times more fertile than spermatozoa from the caput apparently due to abnormalities in locomotion of the sperm cells taken from the head of the epididymis.^{8,24} The percentage of motile bovine sperm cells in the caput and cauda epididymis were 0 and 41, respectively.^{16,17} Staining with an eosin or vital stain revealed equal numbers of live, unstained cells and

morphologically normal spermatozoa in both sites. Spermatozoa removed from the cauda epididymis exhibited normal fertility. Only about 1 ml. of fluid per day flows through the ovine epididymis but the epididymis does secrete compounds such as glycerylphosphorylcholine.⁸

The seminal fluid in bulls is concentrated as it passes through the epididymis, especially in the head region, so sperm cell concentration in the tail of the epididymis in bulls is 4,000,000 or more per cmm. In the epididymis sperm cells exhibit a very low rate of motility and are resistant to cold shock.⁷ In the tail of the epididymis storage conditions are optimal. Spermatozoa can remain viable and fertile for up to 60 days in the ligated epididymis of the bull.⁹ After long periods of sexual rest, however, many spermatozoa in first ejaculates may be dead or infertile. Bulls have about 70 billion spermatozoa outside the testis proper, extragonadal sperm reserves (ESR), with 19 billion (29%) in the head, 5 billion (7%) in the body, 37 billion (53%) in the tail of the epididymides, 2 billion (3%) in the ducti deferentia and 6 billion (8%) in the ampullae.¹ Thus the major storage site for spermatozoa is the tail of the epididymis. Depletion trials in the bull, consisting of 20 or more ejaculates taken within several hours, removed about 53 percent of the extragonadal sperm reserves. In the ram depletion trials reportedly removed only 31 percent of the extragonadal sperm reserves. In the bull these depleted extragonadal sperm reserves are completely replenished within about 7 days and a significant replenishment of spermatozoan numbers in the tail of the epididymis occurred within 60 to 90 minutes after the last ejaculate. During depletion trials no increase in proximal protoplasmic droplets or abnormal spermatozoa were noted.

Unejaculated, defective²⁷ spermatozoa or spermatozoa confined to the epididymis by resection or ligation of the ductus deferens or vasectomy have been reported to be removed from the epididymis, rete testis and efferent ductules by selective phagocytosis by macrophages and epithelial cells or resorbed.^{4,13,20,25,27,29} Histologic examination has only occasionally shown degeneration or phagocytosis of sperm cells in the rete testis or epididymis.¹³ Many workers have reported that spermatozoa were voided in the urine.^{2,21} The number of sperm cells voided daily in the urine of sexually-rested rams was about the same as the total daily sperm cell production. Long term vasectomy in the bull did not abolish spermatogenesis and testis size was unaffected even after 5 years.¹⁸ Thus a mechanism must exist for the removal of sperm cells from the epididymis. Further work is needed to elucidate the fate of unejaculated or defective, dead sperm cells. Masturbation in domestic animals may cause some de-

pletion of sperm cell reserves from the tail of the epididymis. Thus there are apparently several routes for eliminating excess, dead, or abnormal spermatozoa from the testis and epididymis.

The ductus (vas) deferens is a firm muscular duct, about 2 mm. in outside diameter in the bull, that transports spermatozoa by peristalsis especially at the time of precoital stimulation and ejaculation to the ampullae and the pelvic urethra. The ampulla of the ductus deferens, present in the bull, stallion and ram, is a thickening of the ductus abundantly supplied with glands that are similar to the vesicular glands. The ampullae have a limited role in the storage of spermatozoa. There is no noticeable enlargement of the terminal portion of the ductus in the dog, tom or boar.

The accessory glands including the vesicular glands; (seminal vesicles), the prostate; and bulbourethral (Cowper's) glands are under the control of testosterone from the interstitial cells of the testis and secrete the major portion of the seminal plasma into the urethra at the time of ejaculation. The seminal plasma acts primarily as a carrier for spermatozoa and secondarily stimulates spermatozoan activity by providing fructose, a readily available energy source, and buffers. While seminal plasma is capable of influencing the fertilizing ability of spermatozoa there is no evidence it is essential for it.

In 7 vesiculectomized bulls the volume of the ejaculate decreased as did the motility of the spermatozoa while the concentration of sperm cells increased. Five of these bulls were mated with heifers and had acceptable fertility. Seminal vesiculectomy in bulls nearly eliminated fructose in semen and reduced the protein level and ejaculate volume.¹⁹ There was a greater loss in sperm cells after freezing in the treated bulls but the libido was not affected. The vesicular gland secretion is not essential, as the metabolic needs of the sperm cells are provided by the secretions in the female genital tract. In the bull the vesicular glands contribute slightly to the presperm semen fraction but mainly to the sperm cell rich fraction of the ejaculate.¹² The vesicular glands secrete fructose, citric acid, potassium, proteins, enzymes and other substances. Certain prostaglandins have been reported to be present in the seminal plasma of man, guinea pigs and rams. These have a strong pharmacodynamic effect on the smooth muscle of the genital tract of females facilitating sperm migration.³¹ In certain Holstein, Hereford and Guernsey bulls, and possibly in other breeds, the semen may have a definite yellow color due to riboflavin secreted by the vesicular glands. This may be inherited as a dominant character. Upon standing in sunlight for several hours the yellow color will fade.³³ In the boar, secretions from the seminal vesicle and bulbourethral

lands when mixed form a gelatinous, waxy, tapioca-like material. Certain horses, especially grade animals and only occasionally Thoroughbreds, produce a thick, gelairy, "egg-white," sticky secretion from the vesicular glands.^{2,6,11} This is of interest in light of the production of a vaginal plug or coagulum in the rat and guinea pig when Cowper's gland and the secretions from the coagulating gland, a portion of the prostate, combine with secretions from the seminal vesicles.¹⁵ This promotes fertility in these latter species by sealing the vagina and preventing the escape of semen. No useful function of this viscous portion of the ejaculate is evident in swine or horses.

About 50 percent of the volume of semen in the bull and 20 percent in the boar come from the vesicular glands. The prostate gland in the dog and tom provides most of the volume of the ejaculate as in these species the vesicular glands are absent and bulbourethral glands in the tom are fairly small. In the boar the prostate gland is relatively small weighing about 20 gms., compared to the other large accessory glands.

A number of references appear in the literature referring to urethral glands in domestic animals. As indicated previously urethral glands are not present in domestic animals; it is likely that some authors are extrapolating from the human or mistake the disseminate or diffuse portion of the prostate glands around the pelvic urethra for urethral glands. The bulbourethral (Cowper's) glands are relatively small in all species except swine where they provide about 20 percent of the volume of the ejaculate. The clear watery secretions dribbling from the sheath or penis during sexual stimulation in bulls, stallions, and rams are considered to originate from the bulbourethral and possibly the prostate and vesicular glands,^{2,9,12,23} and may assist in clearing and flushing the urethra before ejaculation.

After castration or vasectomy, spermatozoa may be found in small numbers in the ejaculates of stallions, dogs, rams and bulls for up to 21 days, indicating the presence of residual spermatozoa in the ductus deferens and ampullae. In geldings no motile spermatozoa were obtained after 7 or 8 days after castration.³⁰ The numbers of spermatozoa were very low in the ejaculate, 20×10^6 and 40×10^3 in the stallion and dog, respectively. Thus it may be prudent not to allow males to associate with females for 1 to 2 or 3 weeks after castration or vasectomy if pregnancy is to be avoided.²⁶

Erection and Ejaculation

The penis has a twofold function—the expulsion of urine, and the deposition of semen in the genital tract of

the female. Before the latter process can occur the penis must become erect. This is provided for by the erectile structures, the 2 large corpora cavernosa penis and the small corpus cavernosum urethrae (spongiosum) that become distended by blood. In the stallion the cavernous spaces of the corpus spongiosum extend into the glans penis and cause "belling," flowering or great dilation of the glans during erection and ejaculation.^{2,8} Stimulation of the nervi erigentes composed of parasympathetic fibers from the pelvic and sacral nerves results in erection. Erection is accomplished by blood from the internal and external pudendal arteries to the penis and relaxation of the helicine arteries. The cavernous blood sinuses dilate with blood, the outflow of which is retarded or blocked by the contractions of the smooth muscles of the corpora cavernosa and the extrinsic ischiocavernosus and bulbospongiosus muscles at the base of the penis.^{2,1,3,4,5}

The dilation and filling of the bulbous areas of the bovine penile crura under the ischiocavernosus muscle together with 4 or 5 contractions of this muscle "pumps" blood into the corpus cavernosum causing rapid penile erection with the resulting blood pressure peak in the corpus cavernosum penis averaging 14,198 mm of Hg (about 275 pounds per square inch (PSI)), range 8000 to 24,000 mm. of Hg, at the time of coitus and ejaculation in the bull.⁴ Thus if forced ventral angulation or bending of the erect bovine penis at the time of copulation occurs, a dorsal rupture and hematoma may result.² In the stallion the highest peak of pressure in the corpus cavernosum penis was 7,900 mm. of Hg. and the average peak pressure in the corpus spongiosum penis during coitus was 994, range 642 to 1784, mm. of Hg.³ The contractions of the bulbospongiosus muscle at the time of ejaculation forced about 8 waves of blood distally in the corpus spongiosum moving the semen down the urethra.^{2,3} In the buck the corpus cavernosum penis peak pressure during coitus was about 10,000 mm. of Hg and the peak pressure in the corpus spongiosum penis was 750 to 1250 mm. of Hg.¹ Since the high blood pressure in the corpus cavernosum is maintained for only a short period of time, it is suggestive that full erection only persists as long as the ischiocavernosus muscle is contracted and forcing and holding the blood in the penis. The mechanism of the erection in the dog which is aided by the contraction of the vulvar sphincter muscles after intromission¹² has been well-described.^{5,7a} A similar pumping action to that in the bull and buck is noted in the dog and ram.¹² This "pumping" action of the pelvic urethral muscle and the bulbocavernosus muscle causes an intermittent increased blood pressure or wave in the corpus cavernosum spongiosum to compress the urethra to expel semen.

The anatomic structure of the male penis influences

the precoital and coital sexual behavior of the animal.^{7b} The vascular penis in the stallion and dog is slow to erect and foreplay before copulation is essential. The fibro-elastic penis of the bull, ram, and boar, containing much less vascular erectile tissue, erects rapidly and there is less foreplay in these species. The acts of erection and ejaculation are reflex, with the centers being located in the lumbar region of the spinal cord.²⁰ Normally the nervous paths responsible for erection and ejaculation also involve the cerebral cortex of the brain. Erection can take place, however, even if the spinal cord is divided in the thoracic region. Reflex stimulation from the testicles, urethra, prostate, or penis, especially the glans penis, causes erection. Sectioning of the sensory pudendal or dorsal nerve of the penis prevents ejaculation when the glans penis is stimulated. Erection is predominantly under the influence of the parasympathetic system and ejaculation is controlled by the sympathetic system.⁸

Animals such as the stallion, dog, and boar, which ejaculate large amounts of semen have a prolonged period of coitus. The bull, ram and tom ejaculate small amounts of semen and their period of coitus is short. The duration of coitus or copulation in the domestic animals, including erection, mounting, intromission, ejaculation, withdrawal and dismounting is approximately as follows:

Stallion	1 to 3 minutes	Bull	5 to 10 seconds
Boar	4 to 6 minutes	Tom	10 seconds
Dog	5 to 45 minutes	Ram	3 to 5 seconds
		Buck	3 to 5 seconds

Although copulation initiates ejaculation by sensory stimuli from the glans penis, certain stimuli are more important than others in the various species.^{7b} In the bull and ram the warmth of the vagina is most important and pressure and friction less important as stimuli for ejaculation. In the stallion, boar and dog pressure on the penis is relatively more important than temperature.

The non-erect penis of the stallion is about 50 cm. long and 2.5 to 5.0 cm. in diameter and when erect it doubles in length and thickness and the glans penis enlarges 3 to 4 times.² In the bull penile extension from the sheath was about 55 cm. or 22 inches.^{10,11} The interval of time from contact of the glans penis with the vulva to ejaculation averaged 1.0 second. Semen emission time averaged 0.29 seconds. During more than half of the ejaculations by 8 Holstein bulls a twisting of the glans penis was observed ranging from a slight bending to a 360° counterclockwise coil 6 cm. in outside diameter. In the ram the urethral or vermiform process engorges with blood, the urethral dilatation in the base of

the process fills with semen and the semen is forced through the narrow orifice at the end of the urethra under considerable pressure producing a back and forth spraying or "fire hose" effect at the time of ejaculations.⁹ In the boar the corkscrew glans engages in the thick-walled, spiral, transverse ridges of the sow's anterior vagina and cervix that are erect and edematous at estrus. The porcine penis becomes "locked" in the cervix by further erection and dilation of the corpus cavernosum before ejaculation commences.

In the dog two stages of coitus have been described.^{7a} The first stage which lasts several minutes is characterized by intromission without erection, which is made possible by the large os penis, followed by the marked enlargement of the bulbus glandis which is rigidly anchored to the os penis that prevents the withdrawal of the penis from the caudally constricting vestibular structures of the bitch. During this first stage the sperm-rich fraction of the semen is ejaculated. The second stage of coitus lasting 5 to 45 minutes is characterized by the male dismounting and facing in the opposite direction from that of the bitch. This results in an 180° bending of the penis in the middle of its body caudal to the os penis. This act delays detumescence by causing venous occlusion. The major portion of the seminal volume is ejaculated during this stage into the "closed" vagina. This may possibly assist in forcing the semen cranially into the uterus. Human restraint to impose the first stage posture during the entire act may result in reduced fertility.^{7a}

The process of ejaculation starts in the epididymis and travels along the ductus deferens. At the same time the walls of the accessory glands contract and force their contents into the urethra. Sexual stimulation in the bull and possibly males of other species may involve oxytocin release as an increased volume and total number of spermatozoa of the ejaculate followed oxytocin injection.⁶ It would seem logical that oxytocin might be involved in the transport of semen in the epididymal tail and the ductus deferens. The urethra is emptied by the rhythmic contractions of the urethral, ischiocavernosus, and bulbocavernosus muscles.²⁰ The stallion, for example, requires about 10 seconds for complete ejaculation, and about 10 pulsations of the urethra occur approximately a second apart.

Semen and the Ejaculate

Semen or sperm is the entire seminal discharge of the male during normal ejaculation. It consists of cellular elements, or spermatozoa produced in the seminiferous tubules, and seminal plasma or the liquid portion of the

Semen produced by secretions of the seminiferous tubules, epididymis, ducti deferentes, and ampullae, vesicular, prostate, and bulbourethral glands. Sperm cells constitute about 10 percent of bull semen by volume. Two to 5 percent of boar semen is made up of spermatozoa and epididymal secretions. The amount of semen and concentration of spermatozoa varies greatly between species and individuals. (See Table 23.) In species having photoperiodic breeding and nonbreeding seasons variations in semen volume, concentration of spermatozoa, testosterone and LH plasma concentrations and libido occurred between these seasons.^{14,33} Environmental influences had little or no effect on semen output in AI bulls.¹¹ By "teasing" bulls before service the amount of semen and the numbers of spermatozoa per ejaculate can be increased.^{15b} In stallions such "teasing" may increase semen volume but does not increase spermatozoan numbers.^{23b} Some bulls producing a small volume of semen with a low total number of sperm cells in either collection with the artificial vagina or electroejaculation

may produce larger ejaculates with much greater sperm cell numbers if given 50 to 100 units of oxytocin intramuscularly 5 to 10 minutes before collection.

Frequent ejaculation reduces the amount of semen and the concentration of spermatozoa and if carried to extremes, as in depletion or exhaustion trials, marked reductions may occur. These trials have been used extensively as a method of estimating sperm reserves in the live animal. In 44 depletion trials in 21 adult bulls where 20 consecutive ejaculations were collected in an artificial vagina from each bull within 1-1/2 to 7 hours, the average volume of semen declined from 4.2 ml. to 2.1 ml. between the first and twentieth ejaculate. The concentration of spermatozoa decreased from 1.35 billions per ml. to 0.3 billions per ml. and the total average number of spermatozoa per ejaculate decreased from 5.8 billion to 0.65 billion. Except for a slight reduction in semen volume, semen characteristics including concentration of sperm cells had returned to normal within 7 days.⁵ Weekly output of spermatozoa was increased 112 percent in 10

Table 23. Semen Characteristics in Domestic Animals

Semen Constituent	Bull	Stallion	Ram (Buck)	Boar	Dog	Tom
Volume (ml)	4* (1-15)**	70 (30-250)	1 (0.7-3.0)	250 (125-500)	10 (1.0-25.0)	0.04 (0.01-0.12)
Spermatozoan Concentration (millions/ml)	1200 (300-2500)	120 (30-600)	3000 (1000-6000)	150 (25-1000)	125 (20-540)	1730 (96-3740)
pH	6.8 (6.2-7.5)	7.4 (7.0-7.8)	6.8 (6.2-7.0)	7.4 (7.0-7.8)	6.7 (6.0-6.8)	7.4
Total Spermatozoa per Ejaculum (billions) (Approx.)	4.8	8.4	3.0	37.5	1.25	0.057
Fructose (mg/100 ml)	530 (150-900)	2 (0-6)	250	13 (3-50)	0	—
Glycerolphosphorylcholine (mg/100 ml)	350 (100-500)	— (40-120)	1650 (1100-2100)	— (110-240)	180 (110-240)	—
Potassium (mg/100 ml)	140 (80-210)	60	90 (50-140)	240 (80-380)	—	—
Sodium (mg/100ml)	230 (140-280)	70	190 (120-250)	650 (290-850)	90 (50-124)	—
Phosphorus (Total in mg)	80	17	375	66	13	—
Citric Acid (mg/100 ml)	700 (300-1100)	25 (8-60)	140 (110-260)	80 (60-100)	Trace	—
Inositol (mg/100 ml)	35 (25-46)	30 (20-47)	12 (7-14)	530 (380-630)	—	—
Sorbitol (mg/100 ml)	— (10-140)	40 (20-60)	92 (76-120)	12 (6-18)	0	—
Ergothionine	0	(40-110)	0	(6-23)	—	—

Other substances found in seminal plasma include calcium, magnesium, chloride, carbon dioxide, proteins (1-7 gms/100 ml), amino acids (cattle and sheep), lipids, urea, uric acid, lactic acid, ascorbic acid, phosphatase, muco-proteins, fatty acids, vitamins (riboflavin), peptides, other enzymes, hormones, and water (85-98%), * = average, ** () = Range.

bulls by collecting six ejaculates per week instead of two. Bovine semen collected daily showed no difference in ability to store or freeze, fertility, abnormalities of spermatozoa, motility, or pH from semen of bulls collected only once weekly.^{16,17} The volume of semen, concentration of spermatozoa, percent motility and total spermatozoa per ejaculate for bulls collected one time per week vs bulls collected 6 times per week were 9.5 vs 6.2 ml., 1.9 vs 0.8 billion/ml., 63 vs 69 percent and 17.8 billion vs 4.8 billion per ejaculate, respectively. Deficiencies in the quality of semen of abnormal bulls may be revealed by a high frequency of collection but are not caused by a high frequency of collection.^{3,4,5} Semen characteristics were most severely affected by a high frequency of ejaculation in young immature bulls and with sexual rest they took longer to return to normal.³⁴

A study of 350 beef bulls and 870 dairy bulls from 1958 to 1966 indicated that beef bulls comprised a different "population" than dairy bulls.¹⁰ Beef bulls had lower sperm cell production, lower post-freeze motility and higher numbers of abnormal sperm cells (50 percent of beef bulls had above 10 percent abnormal cells). Beef bulls reached puberty one to three months later, and their libido was generally lower than dairy bulls. The period of recovery after ejaculation was not evident in beef bulls as in dairy bulls. Once a beef bull was sexually stimulated 4 or 5 successive ejaculates could be collected in nearly the same time as required to obtain the first ejaculate. Sexual preparation did not significantly increase sperm cell output in the following ejaculate in beef bulls.¹¹

A stallion performed 12 normal services or covers within 72 hours. Two days previously he had ejaculated 50 ml. of semen containing 8 billion spermatozoa. On the twelfth ejaculate 90 ml. of semen containing 4 billion spermatozoa were delivered.¹⁸ In a recent depletion trial in which 5 ejaculates were collected at hourly intervals from 2 to 3 year-old, 4 to 6 year-old and 9 to 16 year-old stallions the sperm cell numbers per ejaculate declined from 4.5, 9.5 and 11.4 billion to 0.5, 1.1 and 1.2 billion respectively in the first and fifth ejaculate.^{14,33} In depletion trials with stallions an average of 20.8 billion spermatozoa were obtained in each trial. After one day of sexual rest 11.8 billion of spermatozoa were obtained in a second depletion trial. With 5 days of sexual rest after the first depletion trial 25.7 billion spermatozoa were collected. Only 2 to 4 collections could be made in each depletion trial with stallions due to a lack of libido.^{8b} Stallions ejaculated daily during the breeding seasons produce about 5 billion spermatozoa per day.

In an exhaustion test a ram ejaculated 42 times in 9 hours and still delivered a total 100 million spermatozoa in the last ejaculate.²⁴

In dogs libido remained high with one to two ejaculations per day. The total sperm cell count per ejaculate dropped from 580 and 548 million in dogs collected 2 and 3 times per week to 286 million and 147 million in dogs collected daily or twice daily, respectively. The total number of spermatozoa per ejaculate returned to normal after 2 to 3 days of sexual rest.⁹

In boars collected once every 4 days and once a day for 20 days the average ejaculate volume dropped from 286 to 193 ml., the sperm cell concentration from 275 to 143 million per ml. and total average daily sperm cell numbers from 55 to 24 billion. No changes were noted in percent motility, percent abnormalities, or pH in the same boars on the two frequencies of ejaculation.¹⁵ There may be a great variation between males in the same species in respect to their ability to copulate frequently and produce a satisfactory ejaculate. (See Table 23.)

In the pig, horse and dog the seminal plasma placed in the uterus during coitus is in contact with the spermatozoa for a period of time in the uterine lumen before some of the latter enter the tubes. While in man, cattle, cats and sheep the sperm cells are in contact with the seminal plasma in the vagina, after ejaculation a relatively shorter period of time before the cells migrate into the cervical canal. In all animals however the seminal plasma is not necessary for sperm cell metabolism or prolonged survival in the female genital tract. The possible role of seminal plasma in the various species has been reviewed.²⁵

Fructose is the normal sugar providing a source of energy for spermatozoa in the semen of the bull, ram and buck, but is low in the boar, very low in the stallion and absent in the dog. It is produced mainly by the vesicular glands. The rate of fructolysis in semen is generally correlated with the concentration of spermatozoa. It is also related to the availability of oxygen and the buffering capacity of the seminal fluid. Spermatozoa can utilize glucose for energy as well as or better than fructose. Sorbitol is a sugar alcohol that can be oxidized to fructose and provide a source of energy. Lactic acid in semen increases as fructose is broken down and may reach levels in the bull and ram where it immobilizes the spermatozoa. The metabolism of sperm cells is characterized by appreciable respiratory activity. Glycerol when added to semen protects spermatozoa during the freezing process but is not readily oxidized by the cells. Of the amino acids in seminal fluid, glycine has been shown to improve sperm cell survival. Glycerylphosphorylcholine is present in high levels in epididymal secretions. By means of a compartmental analysis model in bulls, the mean volume contributions to the ejaculate were 32 to 38 percent (1.5 to 2.0 ml.) from the vesicular glands, 31 to 36

percent (1.7 ml.) from the epididymides, and 31 to 32 percent (1.5 to 1.7 ml.) from the prostate and bulbourethral glands.²⁹

Inositol from the vesicular glands occurs in a high concentration in boar semen where it may act as an osmotic pressure regulator. Ergothionine, a sulphhydryl-containing compound from the vesicular glands, occurs in appreciable amounts in boar and stallion semen. An antiagglutinin that prevents the head to head agglutination of spermatozoa is also found in the seminal plasma. Dog semen contained 7 times as much copper and 20 times as much zinc as corresponding blood samples.⁷ Catalase has been found at low levels in bull and ram semen, 0.3 to 1.1 units per ml., and its addition to bull semen prolonged sperm cell survival by preventing the formation of hydrogen peroxide.¹³

The sticky, gelatinous, tapioca-like material secreted from the bulbourethral glands in the boar make up about 20 to 30 percent of the total porcine ejaculate,³² and may act to help seal the cervix to prevent a backflow of semen during or after ejaculation. In stallions this heavy, glairy, gelatinous substance is uncommon in light Thoroughbred horses but may be present in certain individuals or certain ejaculates in amounts of 30 to 50 percent or more of the total ejaculate.

Most male animals have a low level, below 100 ng/ml. of prostaglandins in the seminal plasma. While the ram, buck and man have higher levels. Their function, if any, has not been determined. Possibly their effect on the smooth muscle of the female reproductive tract may aid the transport of spermatozoa.^{8,8,25}

Ram and bull semen which have a high concentration of spermatozoa are opaque white in color with a creamy consistency. The boar, stallion and dog semen which have a much lower concentration of sperm cells have a pearly white to grey translucent color with a more watery consistency. The difference between species in the volume of semen is largely due to the amount of secretion from the accessory glands.

Coitus and ejaculation are long in the boar and dog, moderately long in the horse, and very short in the bull, ram and buck. In the boar and the dog most of the "sperm-rich" fraction of the semen is ejaculated the first 3 to 6 minutes of coitus. In boars there may be several episodes during the long ejaculation characterized by the passage of "sperm-rich" fluid in between the longer periods in which gelatinous and "sperm-poor" fractions are emitted. The ejaculate of all domestic animals can be divided roughly into 3 portions. The first is a sperm-free, clear, watery secretion probably from the diffuse portion of the prostate or possibly the bulbourethral glands or vesicular glands that may often be observed in some animals in

the precopulatory period of sexual arousal. This is followed by the relatively short period of the emptying of the ampullae of the ducti deferentes and the urethra by the sperm-rich fraction. The third phase or portion of ejaculation is much longer and composed mainly of sperm-poor seminal plasma from the accessory glands. This latter portion in the boar and stallion contains the gelatinous material. In the stallion the last part of this third portion of the ejaculate is spoken of as the "tail end" or "dismount" sample. It is not representative of the entire ejaculate in the horse or in other species. This last phase of ejaculation comprises about 40 to 60 percent or more of the entire volume of the ejaculate. In the bull the pre-sperm fraction is low in fructose and the sperm-rich and post-sperm fractions have a high fructose content indicating admixture with the secretions of the vesicular glands.¹²

Frequency of Service—Since spermatozoan production is a continuous process not affected by frequency of ejaculation, theoretically there should be no limit to the number of services. There are, however, limitations in all males to the number of services possible within a given time. (See Table 24.) As noted previously, frequent repeated ejaculations over a relatively short period of time tend to cause a reduction in sexual desire, semen volume, and number of spermatozoa per ejaculate. Young or immature males should be used conservatively inasmuch as the decline in semen quality is probably more easily produced and undesirable behavior associated with decreased sexual desire might develop.

Each male should be handled, observed, and bred as an individual. In young males a certain degree of size must be attained before coitus can be performed with physical safety. Establishing proper breeding habits in male animals and not permitting these habits to develop in a haphazard fashion is highly important.²⁴ The frustration of small, immature males following unsuccessful attempts to copulate with females that are too large, are improperly restrained, or in an unsuitable location, conditions which may result in slipping and falling, or in head injuries because of a low ceiling, may produce both physical and psychological injury. Both may have a prolonged effect on a sire's attitude toward service. Some males develop sexual desire slowly. Proper development of breeding habits in a male is just as important as training a heifer to milk or a horse to ride. Patience, understanding and avoiding overuse or harmful experiences are necessary for the young male.

In male animals offered frequent opportunities for copulation, libido usually declines before the quality of the ejaculate is lowered to a degree that would affect fertility. In 16 bulls and 8 rams under natural mating

Table 24. Approximate Guide to the Frequency of Service and the Number of Females Allotted to Male Domestic Animals*

Species	Immature Males Hand Breeding		Mature Males Hand Breeding	
	No. of Services/week	No. of Females per Season (year)	No. of Services/week	No. of Females per Season (year)
Stallion	2-5	15-40	3-12	30-120
Bull	2-4	20-60	4-12	80-120
Boar	2-4	10-40	4-10	30-60
Dog	1-2	(20-40)	2-6	30-80
Ram (Buck)	6-12	(30-40)	6-24	40-80

Pasture Breeding		Pasture Breeding	
(No. of Females) per season (year)		(No. of Females) per season (year)	
Bull	10-15	10-25**	
Boar	10-20	20-40	
Ram (Buck)	20-30	40-80***	

*This guide will vary greatly for individual males according to their fertility, sperm producing capacity, degree of libido, age and physical condition. It will also be influenced by systems of management, size of pasture or range and nutrition of the sire and dam. Frequent short periods of sexual rest are desirable.

**This figure is for range cattle with a limited breeding season. For dairy cattle on improved pasture with a year-long breeding season this figure could be increased 3 or 4 times.

***Vigorous yearling to adult rams may breed up to 30 to 40 ewes per month; 3 to 8 percent of goat flocks should be bucks.

conditions, the bulls bred each estrous female an average of 1.73 times with the greatest number of services in a day being 10; in rams these respective figures were 4.03 and 29.³¹ In several matings with one female, libido declined in bulls and rams but finding another female in estrus rapidly restored their sexual drive. Collecting ejaculates 6 × weekly from 1 to 7 years of age greatly increased sperm harvest in AI bulls without harming the bulls' growth, reproductive capacity or fertility.³

The average optimum weekly frequency of semen collection to maintain libido and to secure the greatest number of spermatozoa were as follows: for the bull 4 ejaculations and 30 billion spermatozoa, for the stallion 3 to 4 and 30 billion, for the ram 20 and 25 billion, for the boar 3 and 110 billion, and for the dog 3 ejaculations and 2 billion spermatozoa, respectively.¹⁴ In mature bulls properly stimulated, two ejaculates collected twice per week (4 ejaculates/week) produced over 15 to 18 billion spermatozoa and was a practical procedure in AI studs.

Coital Injuries in Male Animals

Balanitis and posthitis of a severe nature frequently leading to adhesions and inability to protrude or retract the penis are occasionally observed in bulls, especially young bulls with great sexual desire the first few weeks on pasture with cows or heifers. Trauma and infection incurred by frequent service and contamination of the

sheath or by exposure to the IBR-IPV virus in the cows' genital tract may result in severe necrotic and pyogenic infections of the penis and prepuce. Young rams may be similarly affected. This type of infection involving the penis and prepuce will be discussed later in this Chapter.

Injury or Trauma to the Penis—In rare instances in the stallion this may be due to the mare kicking at the stallion and striking the erect penis at the time of service. This may cause a hematoma, paraphimosis, laceration, or rupture of the penis. It is easily avoided by the proper supervision of breeding and by being certain that the mare is definitely in estrus. If necessary breeding hobbles or artificial insemination should be used in nervous, excitable mares. In the bull, occasionally the penis catches on the vulvar lips, in a hymenal remnant, beneath the vulva, or when the bull thrusts and the penis is bent sharply at right angles by the cow suddenly collapsing, a rupture of corpus cavernosum and tunica albuginea or vessels, usually on the dorsal surface of the penis occurs opposite the attachment of the retractor penis muscle. A hematoma is thus produced. This is often spoken of as a "fractured," "ruptured," or "broken" penis. This condition is rare in handbred dairy bulls but is not uncommon in beef bulls on pasture. The diagnosis and treatment of these penile injuries and lesions will be discussed later in this Chapter.

Hemorrhage from the Prepuce and Penis following service may be due to tumors of the penis or to lacerations of the penis or prepuce. In rare instances bleeding

from the urethra may be observed in stallions and bulls. It is usually of unknown origin. Lacerations of distal portion of the boar's penis is not uncommon. It is usually due to bite wounds inflicted by other boars or sows during breeding. Some of these injuries may require local wound therapy but most injuries recover without treatment.^{3b} Several affected boars have had a small vascular outgrowth or polyp in the urethra, that caused blood to be mixed with semen at ejaculation.¹ In several bulls observed by the author irregular-shaped calculi have lodged in the urethra and caused bleeding at the time of service but for a while only slight or moderate symptoms of difficult urination were observed. In young bulls there may occasionally be a small fistula in the glans penis extending into the corpus spongiosum cavernosum. On erection a fine stream of blood comes through the fistula. Some veterinarians have described the presence on the glans penis of blue-red raised areas or ulcers that rupture and bleed. In artificial breeding, rubber bands from the artificial vagina may slip over the penis at the time the bull thrusts. These usually cause deep lacerations or even amputation of all or part of the glans penis if they are not removed promptly. Such an occurrence may be prevented by not using rubber bands on the artificial vagina, or by tying them with cord so they cannot slip off. Occasionally persons trimming preputial hairs on bulls will snip off the tip of the penis if care is not taken to hold the penis caudal to the preputial orifice. Bleeding from the urethra in dogs is frequently a symptom of fracture of the os penis.²

Tumors should be removed. Sexual rest should be given most animals with hemorrhage from the prepuce and penis. In cases of urinary calculi the prognosis is often hopeless for future breeding. When bleeding occurs from the corpus through a fine fistula, sexual rest or surgery to close the defect are indicated. In young bulls observed by the author which bled from a fine fistula or ulcer on the glans penis the fertility of the bulls when bred naturally did not appear affected. Successful incision of the urethra of a few boars and removal of the vascular tissue causing the bleeding has been reported.¹

Miscellaneous injuries at the time of coitus in the stallion may include kick injuries resulting in a ventral hernia, fracture of the hind limbs, or severe orchitis. Breeding hobbles, tying up a front leg and a twitch applied to the mare may be indicated to prevent kicking. Application of heavily padded boots to the mares rear hooves has been used. In all breeds of animals especially the larger ones, the footing of the male should be good and the female restrained properly to prevent the male's slipping and falling, possibly causing gonitis, seen most commonly in the bull; dislocation of the hip; fractures

of the limb or pelvis; fractures of the spine; muscle or tendon strains or ruptures; as well as the harmful psychological effect on the male from falling or injuring himself during coitus. Large females should not be bred naturally to small males unless restrained with their rear limbs or all four limbs in a hole or pit. Occasionally inguinal hernia with strangulation of the intestine may follow service in stallions and cause severe colic within 1 to 3 hours. The author has observed 2 improperly-handled young bulls that fractured the humerus by dismounting from a cow sideways, with the affected front leg caught across the cow's back.

Hemospermia in male animals may be caused by penile lesions or fistulas, urethritis, urethral strictures, and vascular lesions in the mucosa, secondary to infections or injury including stallion rings, lacerations or habronemiasis of the urethral process, strongyle larvae or infectious processes in the accessory glands and urinary calculi.^{1,6a,b} After a diagnosis has been reached, following a careful, complete examination utilizing visual, endoscopic, cultural, radiographic examinations of the urogenital organs, adequate, conservative, possibly surgical treatment, along with sexual rest is indicated. Blood cells in the ejaculate is often associated with low fertility.⁶

Vices of Male Animals

Vices are much more common in male animals, especially in the larger species, than in female animals because many males are improperly handled or abused, closely housed or confined in dark, poor quarters, lack exercise, sunlight, normal surroundings, and associations provided female or other castrated animals. Intact mature males are more aggressive than castrated males or females. Behavioral disorders in male animals are often related to or affect the sex act and may reduce copulatory efficiency. Androgens acting during the early period of differentiation organize neural tissue which mediates later sexual behavior in the male. The time this period occurs in the larger animals is not known but in rats it occurs within 5 or 6 days after birth.

Masturbation or Onanism is observed in male animals of all species. There is little or no evidence that it has any significant effect on fertility or even on libido or desire to copulate. If males are being used regularly and frequently for service the frequency of masturbation declines.

In stallions being raced it is considered to have a detrimental effect on training. Some persons consider accumulations of smegma in the sheath cause irritation and masturbation in stallions and therefore advise regular cleansing of the sheath with soap and water. Regular ex-

ercise under harness or saddle, in a large outside paddock away from nonpregnant females or by providing "company" in the form of pregnant mares will help control masturbation. Owners or veterinarians may also use a stallion (Man-of-War) shield or wire brush suspended just in front of the preputial opening, a metal ("bird-cage") device over the glans or a plastic or adhesive tape ring applied just behind the glans penis to prevent erection and masturbation. These latter ring-like appliances must be removed and penis cleaned once a week and before service or irritation may occur. It is the author's observation that erection is common in the confined stallion but masturbation with ejaculation of spermatozoa is uncommon. He agrees with other authors⁷ that stallion rings are cruel and of questionable value in preventing the loss of spermatozoa. They may be the cause of urethral hemorrhoids and hemospermia. Masturbation as a cause of loss of libido is rare.

In other animals regular exercise in a large outside paddock helps greatly to avoid masturbation. In bulls, rams, bucks or dogs a suture of stainless steel wire tied loosely through and across the preputial orifice may be of value. In the pet dog not used for breeding, castration can be performed. Boars may masturbate by inserting their penis into the preputial diverticulum and ejaculating there, resulting in a condition called "balling up." Once this vice has developed it can only be corrected by the surgical removal of the diverticulum.¹ Young boars in artificial insemination studs should be kept isolated in separate pens to prevent **pederasty** or rectal "copulation" which is common in this species.⁵ It may occur occasionally in young bulls or rams running together.

Viciousness in Males is often a result of confinement and ill treatment. Dairy bulls are usually confined and are much more apt to be dangerous than are beef bulls, that have freedom to run with the herd. Proper, intelligent handling of male animals from a young age, together with regular daily handling, firm training, and exercise makes most males fairly tractable and easily controlled. Since the larger intact male animals are usually closely confined and caretakers are often afraid of them they are very apt to be teased, irritated and handled indecisively which tends to encourage viciousness. Once a male of a large animal species has become vicious and difficult to manage and this vice is well-developed it is a very difficult, dangerous, and often an impossible task to correct these habits without elaborate facilities and intelligent, trained help. Not infrequently following castration a formerly vicious stallion will retain his same disposition unless he is retrained. In this respect the vicious stallion is similar to the vicious "nymphomaniac" mare.

Slowness in Breeding is often an acquired vice in male domestic animals that is favored by improper training, rough or ill treatment or painful accidents that have occurred at the time of copulation. This is discussed much more fully later in the section on impotency under forms of infertility in the male. Many male animals develop idiosyncrasies exhibited at the time of mating that usually have their origin in various restraint practices employed by owners prior to permitting service by the male.

Other vices seen commonly in stallions as a result of close, unnatural confinement are stall-walking, weaving, cribbing and self-biting or mutilation. Stall walking may possibly be controlled by regular exercise, closing the stall tightly, hobbling, or tying the animal, by placing bales of straw around the stall or by putting the stallion in a large outside paddock or pasture. Cribbing should be controlled by a cribbing strap or by radical surgery. Weaving is difficult to correct, but proper exercise, a large and well-lighted box stall, or an outside paddock may be helpful. Using a cradle, a pole between the halter and a surcingle, or a muzzle may be indicated in self-biting stallions if proper exercise and management can't control the vice.

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Nutrition and Infertility in the Male

The nutritional requirements of males are similar to those of nonpregnant females. On the basis of our present knowledge, the qualitative and quantitative requirements for reproduction in the male do not exceed those for the growth of young animals or for the maintenance of mature animals in a state of good health. In bulls, rams, and boars rations that are satisfactory for normal growth to 3 years of age are normal for reproduction.¹¹ The requirements for pregnant, and especially lactating, animals are higher than for the male. In large animals the ration should include good quality roughage. The value of good pasture cannot be over-emphasized. The ration should be properly balanced in carbohydrates, protein, and minerals and supply the vitamins known to be essential for good reproduction. Although numerous attempts have been made to formulate rations that will increase spermatozoan production and semen quality, it still appears that there are no specific nutrients concerned only with fertility.¹² In few fields are there more opinions with less supporting evidence than in the field of infertility.¹¹ A definite deficiency of any single nutrient is seldom found. Natural-occurring deficiencies are usually multiple. The breeding male should be kept in good physical condition and should not be permitted to become overweight. A severe deficiency in nutrients affects the testes in a manner similar to ischemia, hypoxia and hypoglycemia and results in a chronic degeneration of the seminiferous tubules.^{13b}

A low plane of nutrition is frequently encountered in practice. As physical deterioration progresses into inanition in the male there occurs an atrophy of the testes, a decrease in the number of spermatozoa per ejaculate,

and a progressive loss of sexual desire. Delayed puberty will occur when there is a low plane of nutrition in the young male animal.^{2,4} Underfeeding during the growth period had a limiting effect on sperm cell production at maturity in bulls.¹⁵ Thus a low plane of nutrition may adversely affect reproductive functions in the male but severe effects on reproduction are not observed unless emaciation and inanition are marked.

A high plane of nutrition is frequently cited as a cause of infertility, especially in fat, overfed, obese, show animals. There is no experimental evidence that a high level of feeding and body condition has any effect on semen production. Fertile rams fitted for show continued to be fertile even though in a very high state of nutrition.⁸ Obesity did not increase rectal or scrotal temperatures or cause any degenerative changes in the testes. Some authors have suggested that certain male animals develop excessive fatness because of an endocrine disturbance such as hypothyroidism, that predisposes the male to infertility. This is possible but it has not been proven. Phlegmatic, lazy bulls tend to put on excessive weight. Rearing intensity did not affect a bull's mating behavior.¹

High body condition may result in slowness, difficulty or inability to copulate because of paunchiness, laziness, weaknesses in legs and feet and a lack of sexual desire in some males but this is not associated with defective spermatogenesis.⁴ Excessively fat bulls may possibly have enough fat around the testes in the scrotum, especially the dorsal part, to insulate the testes and affect spermatogenesis but this has not been proven. Some very fat beef bulls are highly fertile. In some bulls excessive fat in and above the scrotum may be confused with an inguinal hernia. When the obesity in these males is corrected by limited feeding and increased exercise the inguinal fat is slow to disappear. Therefore high energy intakes are not desirable for bulls past the stage of rapid growth but moderately heavy early feeding may promote early semen production by hastening the onset of puberty.

Feed Constituents. Under the usual conditions of management the possibility of deficiency in either the quality or quantity of protein fed to males seems remote. When the protein in the ration was below 2 percent, low feed intakes, loss of weight, weakness and reduced libido and sperm cell production occurred in rams and bulls.^{9,16} Urea was satisfactory as source of protein in ruminant male animals. Although some veterinarians have recommended feeding animal protein such as skim milk, fish meal, turkey mash, or other high-quality protein pellets, there is no evidence that it is necessary, providing adequate grain and good roughage are available.

Vitamin deficiencies are seldom observed as a cause of infertility in the larger male domestic animals if the roughage in the ration is near normal in quality or quantity. Vitamin A deficiency, if severe and characterized by night blindness and stiffness, may cause cessation of spermatogenesis and atrophy of the seminiferous epithelium and a decline in semen quality as well as a decrease in sexual desire. In young bulls vitamin A deficiency may result in cystic pituitary glands.^{3,5,13b} Thirty-five to 100 micrograms of vitamin A per kilogram of body weight daily is ample for reproduction in bulls.¹¹ There is little evidence that deficiencies of vitamins B, C, D, or E are even occasional causes of infertility. Although vitamin E is essential for reproduction in the rat there is no proof or indication that it is necessary for reproduction in domestic animals.^{13b}

Mineral deficiencies affecting reproduction in male animals are rare. Deficiencies of calcium, manganese, zinc, iodine, potassium and selenium have not been proven to be causes of male infertility.^{10,13b} Deficiencies of cobalt, iron, zinc and copper may cause anemia, lack of appetite and loss of weight, and thus have an adverse influence on male reproduction. These trace minerals, especially zinc which is high in concentration in ejaculates of animals, are essential constituents of enzymes.^{13b} A lack of phosphorus, often associated with a lack of protein and low levels of vitamin A under natural conditions may cause reduced appetite, a loss in condition and reduced reproductive function. Osteopetrosis with accompanying spondylitis and arthritis in the bull may result from ultimobranial body hyperplasia or neoplasia caused by excessive dietary calcium.^{6,7} Arthritis and spondylitis may cause hesitancy or refusal to copulate. High dietary calcium levels may be caused by feeding alfalfa or clover hay and dairy grain rations fortified with minerals needed by lactating cows but not by bulls.

Most reproductive disturbances related to nutrition are caused by underfeeding. If the males is fed a normal balanced ration that will produce normal growth or maintain normal health, reproduction will not suffer because of nutritional deficiencies. In some areas owners feed special fortified rations to breeding males. These special fortified rations have added amounts of various types of protein, vitamins, especially vitamin A and beta-carotene, manganese, cobalt, phosphorus and other minerals that when fed amply supply their supposed needs for a high level of reproduction. The necessity or value of these feeds is highly questionable.

Along with proper nutrition and adequate water and salt, factors such as exercise, sunlight, pasture, and other environmental influences, including parasite control and routine vaccinations, play an important role in maintain-

ing the health and activity of the breeding male and in prolonging his usefulness.

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Hormonal Causes of Infertility and Related Syndromes in Males

In male animals there is no infertility condition due to a hormonal cause that uniformly responds to endocrine therapy. Therefore hormonal treatments for lowered fertility or impotency are usually disappointing and of questionable value.

A lack of sexual desire or libido and reduced spermatogenesis with testicular atrophy may be caused by a failure of ICSH, LH and FSH to be released from the anterior pituitary gland by factors originating in the hypothalamus. There are many "stress" factors, the most important one being inanition due to a low plane of nutrition, that may cause this failure. In rare cases, especially in dogs, tumors in the pituitary area may cause atrophy of the pituitary gland and failure of gonadotropin production. More satisfactory response to treatment will follow a correct diagnosis of the cause or causes of a lack of libido or reduced spermatogenesis than the use of gonadotropic hormones in an empirical manner. Because of their protein constitution animals become refractory to repeated doses of gonadotropic hormones. Successful results following their use is usually fortuitous and can usually be explained by other therapeutic or management practices.

If the pituitary gland is functioning normally and releasing ICSH, failure of libido is seldom caused by a lack of testosterone produced in the interstitial cells of the testes. Occasionally in young males, testosterone injections may hasten sexual maturity and improve sex drive. Even abdominal cryptorchid testes produce normal amounts of testosterone. Rarely Sertoli cell tumors in dogs and other males may produce sufficient estrogen to suppress the release of ICSH and cause impotency. Testosterone has been used empirically in bulls with abnormalities of spermiogenesis or evidence of an abnormal environment in the storage of sperm cells in the epididymis. As with gonadotropins; testosterone is seldom successful in the treatment of a lack of sex drive in adult intact males. Thyroidectomy in bulls and stallions resulted in lethargy and mild signs of impotency.^{8,9} Hypothyroidism may be present in some obese, lethargic males. Hypothyroidism in male animals has not been proven but a few fat males fed iodinated casein or injected with thyroid hormone have lost weight and become more alert with an improvement in libido. Thyroxine therapy has little or no effect on spermatogenesis and is not uniformly or highly successful in males lacking sexual desire.

Some bulls with low fertility have fascicular cortical nodules in the adrenal that apparently convert progesterone into large amounts of cortisol.³ This results in a high concentration of spermatozoa and a low fructose concentration in the semen.

Cryptorchidism is considered to be an inherited defect resulting in a failure of the fetal or neonatal testes to descend into the scrotum. The male is usually castrated or slaughtered. In humans cryptorchidism has been treated before puberty by gonadotropins or testosterone with very limited success. Most attempts to use hormones to induce descent of the testis have failed.¹

As discussed previously in this Chapter, testosterone is released from the interstitial cells of the testis in a pulsatile or episodic manner about 7 or 8 times a day under the stimulation of LH (ICSH) released from the anterior pituitary gland by GnRH from the hypothalamus. For this reason the plasma concentrations of testosterone vary in stallions during the day from 65 to 1600 pg/ml.² Geldings have a level basal concentration of plasma testosterone of about 12 to 20 pg/ml. The injection of HCG, 10,000 IU, into a gelding has only very slight effect on plasma testosterone concentration. If HCG is injected into a stallion or cryptorchid ("rig") or a male that has one or both testes retained in the inguinal canal or abdominal cavity, the plasma testosterone concentration rises within one-half hour to 290 to 3750 pg/ml., average 1450 pg/ml.² This dramatic prompt rise in plasma testosterone concentration in the true "rig" or cryptorchid horse either one-half to one hour after the injection of HCG, demonstrated by pre- and post injection blood samples, is an excellent diagnostic procedure to conduct on horses that have no observable testes yet have strong male behavior. This test may also be supplemented by determining the plasma concentration of estrogen which is elevated in the stallion and equine cryptorchid due to the presence of sertoli cells that secrete estrogen. HCG injection however has little effect on the plasma estrogen concentration. Estradiol concentration in the plasma of stallions and geldings was 30 to 60 and 5 to 10 pg/ml, respectively.¹⁶

Treatment of stallions with 200 mg of testosterone propionate IM every other day for 88 days or with anabolic steroids, boldenone undecylate, 1.1 to 4.4 mg/kg or nandrolone decanoate, 1.1 mg/kg IM every three weeks for 15 weeks caused a decrease in spermatozoal concentration and motility, a decrease in total sperm per ejaculate and a reduction in scrotal width and testicular size as well as a depression in the plasma LH concentration.^{13,14,15} These treatments had no effect on sexual behavior, libido, or seminal volume or character. Even though these adverse effects were reversible and normal reproductive parameters returned by 90 days after cessation of treatment, testosterone or anabolic steroid ther-

apy is contraindicated in stallions.^{13,14,15} Libido and ability to ejaculate were gradually lost after castration of stallions. Testosterone restored both these aspects of sexual behavior. Estradiol at a high dosage restored libido however the ability to ejaculate was impaired in geldings.¹⁶

Prostatic hyperplasia in old male dogs is due to excess testosterone produced by the testes and can be alleviated to some extent by injections of estrogens. A more satisfactory method is castration, which removes the source of testosterone in the body. Prostatectomy is difficult and only seldom performed in dogs. Estrogenic therapy is often temporarily successful because it inhibits secretion of the gonadotropic hormone FSH and LH, from the pituitary gland necessary for androgen production from the interstitial cells in the testes resulting in atrophy of the prostate gland. No function has been ascribed to oxytocin in the male but it is most likely concerned with sperm transport and ejaculation. The oxytocin levels in the plasma of men and women are similar.¹²

Zearalenone, an estrogenic mycotoxin, from moldy corn, besides producing effects in the female pig previously discussed, caused reduced libido and depressed plasma testosterone and LH concentrations in young prepubertal and pubertal boars.¹ At the level of zearalenone fed to the treated boars no adverse effects on body or testis size or sperm production was noted even though sexual behavior was delayed.¹

Castration of male animals greatly reduces intermale aggression, and male sexual behavior including mounting, and in dogs and toms reduces urine marking or spraying, and objectionable roaming. In bucks and boars castration eliminates the male sex pheromone odor which is testosterone dependent. Progesterone therapy will frequently improve patterns of problem behavior in castrated or intact males and spayed females. Long-term therapy in males and females, especially the latter should be avoided because of possible side-effects such as mammary tumors or metritis.⁴ The doses recommended for dogs and cats are 2.2 to 11 mg/kg of medroxyprogesterone acetate (**Depo-Provera**) IM or SC or 0.5 to 1.0 mg/kg of megestrol acetate (**Ovaban**) orally. About 50 percent of behavioral problems improve significantly with drug therapy. Like castration results of therapy depend on species, environmental background and individual genetic differences.⁴ The author has used megestrol acetate and repositol progesterone, 500 mg., or progesterone in oil 200 to 300 mg. IM every 24 to 48 hours to reduce undesirable sexual behavior in stallions prior to transport, showing or other activities.

A recent study has demonstrated that **active immunization or ram, lambs and bull calves, against GnRH (LH-RH)** can be produced by an adjuvanted product

injected subcutaneously at 4 to 6 week intervals. This resulted in reduction in size or atrophy of the testes with low plasma gonadotropin and testosterone concentrations after 13 to 15 weeks.⁷ Further studies are necessary to develop this procedure to the point it may replace castration. Many recent studies have been undertaken to produce immunoneutralization with active or passive immunization with antibodies to steroid and gonadotropic hormones. These studies which have been reviewed^{7b} show promise of producing significant future advances in reproduction control in animals.

The **bulling syndrome** in feedlot steers is a major problem for feedlot operators. Of 55,000 steers in one study, 1907 or 2.9 percent became bullers and resulted in an annual loss of about \$325,000 due to injury and the need to isolate affected individuals.¹¹ The use of hormone implants to stimulate the growth rate was shown to be related to the incidence of bulling with a higher incidence with a combined progesterone and estradiol product.¹¹ However this syndrome is observed in feedlots not using hormonal growth stimulants. It is not related to hormonal levels or elevated estrogens in affected animals.⁶ The "buller" syndrome is apparently the result of management factors together with the inherited normal bovine male sexual behavior that usually is suppressed and not exhibited in more isolated steers. Under feedlot conditions the addition of outside, strange animals, irrespective of pen space available, causes an increase in the occurrence of bulling. Since a major stimulus to bovine male sexual activity and libido is to observe another male mount an animal, other steers become aroused and often wait their turn in line to ride the submissive or "chosen" steer.⁶ This latter animal very likely is a passive non-aggressive steer at the lower end of the "peck order."

Endocrine therapy for infertility in males is seldom indicated. It is usually used as a secondary or supportive line of therapy. It is improper and illogical to administer only hormones such as testosterone, thyroid products, or gonadotropic hormones in impotency, or gonadotropic hormones or thyroid products in cases of low fertility, and expect satisfactory results. A good history and careful clinical evaluation of the male should be made to determine, if possible; the etiology of the impotency or infertility, so that intelligent recommendations and treatments can be made. If hormones are used for therapy in male animals their limitations should be recognized.

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Forms of Infertility in the Male

According to Lagerlof these forms may be divided into three general categories:

I. Reduced to Complete Lack of Sexual Desire and In-

ability to Copulate (Impotentia coeundi).

II. Inability or Reduced Ability to Fertilize due to Pathology of the Testes, Mesonephric Duct and the Accessory Glands (Impotentia generandi).

III. Miscellaneous Diseases Affecting the Reproductive Organs.

These conditions are present in males of all species. The degree of each condition present in males varies considerably between species, breeds, families, and individuals. Variations also occur due to age, season, nutrition, management and other factors. There are many degrees, from mild to severe, in each category of the various forms of infertility; a fact which demonstrates strikingly that in males there is a wide range of reproductive ability. Sometimes reduced sexual desire and ability to copulate may be associated with reduced fertility and poor quality semen but in most cases of infertility in males the two conditions are not related. In male animals semen collection is usually possible so that direct measurements of sperm quality and other tests may be applied. In examining males for infertility or sterility, accurate breeding and health records on the male and the herd should be obtained and examined. Secondly, there should be a careful, painstaking physical examination of the male including the observation of his mating behavior. Thirdly, one or more thorough semen examinations by a trained veterinarian or qualified laboratory are necessary. To evaluate the nature of a male's infertility and sterility so that proper recommendations for therapy, treatment, or rest or disposal of the animal may be made, all three of the above examinations are essential. The prognosis in nearly all forms of infertility or sterility in male animals should be guarded.

Reduced To Complete Lack of Sexual Desire and Inability to Copulate (Impotentia Coeundi)

Potency is the physical capability of the entire body to coordinate and perform the male's normal role at coitus including erection, mounting, intromission and ejaculation. A lack of potency is observed in certain males in all species and is characterized by symptoms ranging from a complete lack of sexual interest and inability to copulate to a slight slowness or delay in exhibition of libido, mounting and copulating. Mating and copulatory behavior of males has been reviewed in various species:^{12,18} in bulls,^{5,9,14,19,20,27} in stallions,^{36,37,39,45,46} in rams,^{9,23-26,40,41} in dogs,²⁹ in bucks,^{42a} in toms^{42b} and in boars^{9,28} (see Chapter 12). In the female animal repro-

ductive behavior is relatively simple requiring only a willingness to stand to be mounted, or an attitude of immobility and acceptance. This attitude is primarily under the control or influence of estrogen which may be enhanced by progesterone. In the male animal reproductive behavior is more complex requiring identification, seeking out, teasing and then the performance of the complicated act of copulation. This is under the control or influence of testosterone and other central nervous system mechanisms. There is little relationship between blood testosterone concentrations, libido and semen quality or quantity.^{7,9,11}

The components of the act of copulation consist of sexual excitement, courtship, erection, mounting, intromission, ejaculation, dismounting and refractoriness. There is great variation in the duration of these components between species and individual males within a species. Mating behavior depends to varying degrees on visual, olfactory, auditory, and tactile cues. In all species visual and tactile cues are most important in the actual act of copulation. In the dog olfactory clues are highly important in locating females in estrus. In sheep and swine and to a lesser degree dogs and horses the estrous female actively seeks the male. (See Coitus in Chapter 12.) Even blind males may copulate if experienced.

Height, width, and color of the female, attitudes of acceptance, such as her stance as the male approaches, reaction of the female to pressure of the bull's head on her rump or back, pressure of the shoulder on the mare's rump or biting of the skin of the mare's rear parts by the stallion and by the boar's snout lifting the sow's rear quarters, possibly odor of the rear parts and urine in horses and cattle and sheep utilizing the **flehmen reaction**, which is characterized by the lifted head, outstretched neck and curling of the upper lips that facilitate the introduction of odors or pheromones from the urine or genitals into the vomeronasal organ, and vocalization by the stallion, boar, ram and buck are all significant factors in the pre-copulatory and copulatory acts of domestic male animals.

Sex drive, libido, sexual desire or potency of the male is largely determined genetically but environmental influences play an important role in modifying it.^{2,9,22,23,41,44,47}

It is well known that males differ widely in their ability to copulate frequently. In male guinea pigs, rams and bulls it was demonstrated that those with strong sex drive before castration returned to a strong sex drive when treated with increasing amounts of testosterone after castration whereas animals with a weak sex drive returned to a weak sex drive.^{6,7,9,11,15} It was postulated that the differences between animals were due to the reactivity of their tissues, such as the brain, rather than to the dif-

ferences in the amount of hormone secreted or present in the body. Thus variations in endocrine function may be linked with changed reactivity in the target organs and receptors especially the central nervous system, as well as in the hormone-producing organ.

Many of the complex components of copulatory behavior are determined by hormone action during various stages of development and may persist after castration.^{7,15,22} Studies on identical twin bulls showed many similarities in copulatory behavior between brothers but large differences between pairs.² A significant relationship between the degree of libido in father and son groups of Swedish Red and White bulls was reported.²⁷ Sex drive also varies between different lines of bulls within a breed.⁹ Herefords, Shorthorns, Guernsey and North Devons are genetically slow breeders.^{9,47} It is extremely difficult to evaluate the libido and mounting ability of Brahman, Zebu or Santa Gertrudis bulls since these breeds copulate mainly at night and rapidly so the copulatory act can only rarely be observed.^{9,35} Low libido in Zebu bulls was not associated with a deficiency of LH or testosterone.⁹ It may be necessary in these breeds to place a bull with non-pregnant cycling cattle and then check them for pregnancy in 40 to 80 days or to use the chin-ball mating device (Frank Paviour Ltd. Hamilton, New Zealand) to determine if the bull in question mounted cows in estrus. This latter device marks a cow's back as the bull's chin rubs over it during copulation. But European breeds, especially the dairy breeds, will actively mount confined bulls, steers, and cows in any stage of the estrous cycle. Excessive ambient temperatures may have an adverse effect on sexual activity in boars and bulls.^{9,14,28}

Innate virility is reflected in the number and frequency of copulations that occur in a period of time and these vary widely between males. One study reported on two bulls one of which ejaculated over 40 times in 4 hours and another bull under similar conditions that ejaculated only 10 times.¹ With a new stimulus animal or mount the first bull produced over 30 more ejaculates within the next hour. Some virile rams copulated an average of 20 times a day over a 7-day period whereas rams with low libido averaged only 4 copulations per day.²³⁻²⁶

When bulls with high and medium libido, 9 to 10 services vs 2 to 3 services within a daily 7-1/2 hour pasture mating period, were pasture bred at a ratio of 3 bulls to 114 cycling heifers for 3 weeks, the conception rate on first service was 77.5 vs 59 percent respectively for the high and medium libido bulls. By six weeks the difference in conception for the two groups was only 2.3 percent. Thus bulls with high libido when exposed to large numbers of fertile heifers produced earlier conception.⁶ When only 10 to 12 ewes were single-sire mated to rams

with either high or low libido there was no difference in conception rates.³⁴

Depending on the degree of injury, the age of occurrence and the degree of socialization permitted,^{22,24} lesions of the medial preoptic area of the brain can impair male copulatory behavior in animals. Although libido is genetically influenced, mating ability has a learning component essential for its full expression. **Sexual inhibition of males** is seen in all species of animals where rearing or management systems have prevented or reduced socialization, especially in the young male, by isolation either singly, as may occur in valuable show animals, or in bachelor or all-male groups.^{9,29,33,41} In these all-male groups homosexual behavior is common. Furthermore in all-male groups the dominant males intimidate the weaker more submissive males. Thus the latter lose their male aggressiveness, become sexually "inhibited" and may in the future be an undesirable or "problem" male requiring careful reconditioning, training or culling.

In pasture-bred herds or flocks, social ranking or dominance in males occurs. This is largely controlled by age, seniority and size, not by testosterone concentrations in the plasma or degree of libido.^{5,9,40} These dominant bulls or rams if infertile or lacking in libido could markedly decrease the conception rate since they prevent the less dominant or subordinate males from breeding and spend more time in this activity than in breeding cows. If bulls of different ages are used for natural breeding on pasture or range, the owner should consider dividing the females into smaller single-sire groups to obtain the highest fertility and to avoid injuries to males.^{5,9} This is favored by the observation that most pasture-breeding bulls rarely serve the same heifer twice. Also new females coming into estrus were more attractive to males and could promptly restore libido in bulls and rams apparently satiated by formerly-bred females that might still be in estrus. A study of the effects of the male to female ratio and single- vs multiple-sire groups on efficiency of bulls in natural service revealed that although a few bulls were unable to adequately service large numbers of cows, most bulls with acceptable semen quality, libido and mating ability would achieve good pregnancy rates at a ratio of 1:44 or 1:60 females.^{8,40a} A bull to female ratio of 1:25 was inefficient in realizing a bull's breeding potential. In multiple-sire groups social ranking affected the number of females mated by each bull with subordinate bulls mating fewer females. It was difficult to identify bulls with acceptable libido and mating ability before the pasture breeding season.

In over 2000 rams the incidence of sexually-inhibited rams reared separate from ewes when they were first

placed with ewes was about 30 percent. Within a few days 80 percent of this inhibited group of rams developed normal libido and sex drive. In about 2000 stallions examined each year for 3 years a low incidence of 0.34 to 1.07 percent of stallions with a lack of sexual desire or libido was reported.^{4,37,39,45} Impotency is not uncommon in stallions and is occasionally characterized by normal intromission and failure of ejaculation or abnormalities of ejaculation.

About 16.7 percent of 625 beef sires of English breeds selected by artificial insemination studs were disposed of because of problems in the collection of semen, mainly refusal to serve an artificial vagina.³⁸ Very few Brahman or Zebu bulls will mount and ejaculate into an artificial vagina. Selection of bulls for their femininity, docility and gentleness tended to favor the selection of bulls with reduced desire.³² However in one study with Santa Gertrudis bulls there was no relationship between masculinity and libido scores.^{8,9}

Although sex drive, mating behavior or libido is largely genetic in nature it is subject to great modification by many environmental or physical factors. Males with a strong sex drive require more severe and prolonged environmental and physical insults to significantly affect their mating behavior than do males with a weak sex drive.

Environmental Factors Affecting Sex Desire and Copulatory Ability: Nutrition—Thin, emaciated, semi-starved males or those suffering from deficiencies of TDN., vitamin A, protein, and certain minerals such as phosphorus, zinc and cobalt may have a reduced sex drive. If inanition is severe enough, a complete lack of libido results. As indicated previously a low level of energy intake in growing males retards puberty and the onset of libido.

Overfed males tend to become obese and lazy and often suffer from joint and foot troubles related to their overweight condition. Excessive roughage fed to older bulls and rams may cause great enlargement of the rumen and abdomen interfering with normal, easy copulation and contributing to a lack of sexual desire.

Male animals should be fed a properly balanced nutritive ration in adequate amounts to maintain a fair to good body condition. Exercise is important in maintaining active, healthy male animals.

Systemic diseases—Any chronic or acute, severe, debilitating disease resulting in rapid or prolonged marked loss of weight, or in anorexia, depression, and weakness will cause a varying degree of loss of sexual desire. These diseases may include: pneumonia, enteritis, tuberculosis, paratuberculosis, severe mange and pediculosis, actinomycosis, lymphocytoma, progressive fat necrosis,

severe internal parasitisms, advanced metastatic tumors, alveolar periostitis, traumatic gastritis, severe chronic peritonitis, anaplasmosis and others. In anaplasmosis the loss of libido was associated with anemia and low hemoglobin and packed-cell volume. All bulls, especially in an AI stud, should be given magnets orally at about one year of age to prevent traumatic gastritis or pericarditis.¹⁰ Routine vaccinations of males vs the common infectious diseases of each species is indicated. Early and prompt diagnosis and treatment of all diseases of male animals is imperative to prevent possible loss of reproductive ability.

Age—Very young males or old males frequently exhibit a reduced-to-complete lack of sexual desire. In older animals this may be due to a possible decline in testosterone levels, to senility, to a loss of condition, to overuse or to arthritis. In experiments with identical twins it was shown that the time of onset of the lack of sexual desire in older bulls seemed to be largely determined genetically.²

There is a great deal of variation in young bulls in the onset of sexual desire and puberty. That this may be modified significantly by the nutritive level has been well-demonstrated. High feeding levels hasten the onset of puberty and sexual desire whereas low or subnormal feeding levels greatly retard the time at which the young male shows sexual desire and will mount and copulate with females.

Management practices—Libido will vary within animals depending upon their inherent sex drive and the way they are trained, handled and managed. Young males which are isolated apart from others of their species are frequently frightened by the presence and activity of females and other males and are slow to mount and copulate because of their inexperience and timidity. This is not uncommon especially in bulls, rams, stallions and dogs. Young males should be carefully patiently and quietly trained and handled, especially if they are to have their semen collected in an artificial vagina. If a male associates "sex" with pain or punishment, he may decide to give up "sex"! Males with a lack of libido or naturally "slow breeders" can be easily discouraged and made slower by the insertion of a nose ring in a bull, harsh or abusive handling of the male by attendants, improper restraint of the mount animal, improper footing, mount animals that are not in estrum or are too tall or wide, use of an artificial vagina that is too cold or hot, improper preparation of the male for mounting, breeding large males in a confined area with a low ceiling, unskilled persons using an artificial vagina, and excessive use of a male. Males lacking libido if continually used on the same female for semen collection frequently develop sexual in-

difference or satiation. Frequent changing of the stimulus or mount animals and the breeding site are indicated in bulls inclined to show a lack of libido. The presence of other males near the mount animal or in sight of the breeding male provides further stimulus.^{20,21} Proper sexual preparation of dairy bulls by prolonging the period of sexual stimulation beyond that adequate for mounting and ejaculation will produce higher quality semen with 36 to 250 percent more spermatozoa in the ejaculate.^{20,21} This is accomplished by a longer period of restraint before permitting copulation, frequent changing of the mount animals, allowing several "false" mounts where copulation is not permitted, and moving the male to several different sites for "teasing" or "stewing." Olfactory stimulation has not been demonstrated to play an important role in the sexual behavior in bulls.¹⁹ Some stallions and jacks with low desire will fail to copulate with mares that are well-scrubbed and their tails bandaged. Others will so vigorously bite the withers and neck of the mare after mounting that erection is lost. Muzzling of these males or placing a heavy pad or blanket over the neck and withers of the mare is indicated. Other stallions will perform intromission and make thrusting movements but fail to ejaculate. This is common in stallions with reduced libido that are being used too frequently for their reproductive capacity.^{36,39,45} This failure to ejaculate can be noted by careful observation of the male at copulation by the absence of the usual "flagging" of the tail, which can be misleading, the absence of "pulsations" of the penile urethra felt by manual palpation during coitus, the failure of the stallion on dismounting to be "content" and "relaxed," and also the lack of spermatozoa in the "tail-end" sample of the ejaculate collected from the penis as the stallion dismounts.

Psychic factors interfering with normal coition and resulting in impotency have been observed in males of all species, especially stallions.³⁶ Males with a genetically lower sexual desire are much more apt to develop psychic refusal to breed. Usually there is no obvious clinical reason for this failure but if a good history is available it often reveals a traumatic, painful experience or several of them at the last few attempts at copulation.^{30,36} Some bulls and stallions with apparent psychic impotency may actually be afflicted with lesions of the spinal column as described in the next section.^{13,36} These bulls would apparently have good sexual desire, mount rapidly, have lordosis in the lumbar region and the penis would be directed at the escutcheon well below the vulva. Rapid pelvic thrusts and "seeking" motions would occur but penile exposure was greatly reduced. A prolonged period of sexual rest, a change in the site of copulation and careful preparation may be necessary to encourage

the male to again start to breed. Shy or slow breeding boars may also be observed.⁹

Males should be properly handled and exercised to maintain optimum physical condition. They should be observed and managed so as to prevent their being bred excessively and losing their sexual desire. The frequency of breeding or the individual capacity of each male should be determined. If the male is bred repeatedly over a short period, this should be followed by a period of sexual rest. These above management factors should encourage the timid, slow breeding male, and control and conserve the vigorous active male.

A reduced libido or sex drive in stallions is usually an important cause of concern for the owner(s) because of the value of the animal and the mares presented to him and the loss accrued from failure to impregnate most of "booked" mares within a breeding season. Furthermore in the stallion electro-ejaculation is presently not possible and artificial insemination is limited to certain breeds. The lack of libido in the stallion not only encompasses his reluctance to tease, mount and obtain intromission but many "inhibited" stallions will fail to ejaculate even though a visually normal copulation occurs. The third associated condition in the stallion that is not reported in other male domestic animals is the occurrence of a functional disturbance of the neural mechanism controlling ejaculation. This may result in a normal ejaculation of seminal fluid from the accessory glands without the ejaculation of spermatozoa from the tail of the epididymis and ductus deferens, azoospermia, or the release of urine into the ejaculate usually after the second or third jet of normal semen. No lesions have been found to explain these functional or possibly psychic causes of reduced libido and failure of ejaculation in the stallion.^{36,37,45} It has been noted that "belling" or "flowering" of the glans penis of the stallion following erection is necessary for ejaculation. However if a normal erection does not occur, ejaculation can often be obtained by using an artificial vagina³ without "belling" or "flowering" of the glans.

Psychogenic impotence is common in stallions because they are often reared in isolation, given little freedom for socialization with other males and females during puberty, vigorously trained and disciplined firmly for exhibiting normal male sexual behavior during puberty and their early formative years and are expected to perform instinctively and repeatedly the complete sex act promptly on being retired to stud duty. The most common causes for impotency or lack of libido are overuse as a young stallion, injury during service from being kicked by the mare, and excessive discipline or chastisement during the sexual act. Overuse in older horses

may cause reduced libido but they respond to sexual rest, while too often effects of overuse of a young stallion may be permanent.³⁶ Impotency in a stallion may be manifested by indifference or excessive aggression toward the mare or the handler. The latter aggression is apparently caused by definite signs of frustration on being unable to ejaculate. The author observed this in one older stallion that was aggressive toward the mare, obtained intromission repeatedly, sweating profusely, and emitted a definite "squeal" of frustration on each withdrawal and dismount.

Tests for the Measurement of Libido

Since libido or potency is a highly significant component of the fertility of male animals but is difficult to assess easily and accurately, a number of test procedures have been developed and used.^{6,9} These include:

- 1) the percentage of times that copulation and ejaculation occurred when a male is exposed to a suitable "stimulus" on different occasions, (either by natural service or collection with an artificial vagina)
- 2) the comparative number of completed or uncompleted copulations in a given time period with a "stimulus" female
- 3) observation of the time elapsed between exposure of a male to a "stimulus" animal and the first copulation (This is called the "reaction" time)
- 4) assessment of the ability of a male (bull) (ram) to mount a restrained nonestrous female and ejaculate into an artificial vagina 3 times within a limited time (10 minutes)
- 5) assess the degree of sexual behavior or libido in beef or range-type bulls placed in a small enclosure with a stimulus or ovariectomized, estrogenized heifer (Up to 11 categories of behavior are listed)
- 6) using a "serving capacity test" by utilizing restrained nonestrous cows at a ratio of 5 beef or dairy bulls to 2 to 3 cows and noting the number of services by each bull within a forty-minute time period.

To be of diagnostic value these tests should be conducted under controlled conditions by experienced observers. Some of these tests are not adaptable for use in individual or small herds.

Hypothyroidism, hypogonadism, or a pituitary deficiency causing a diminished secretion of thyroxine, testosterone, or gonadotropin has not been described or proven by radioimmunoassays in normal intact male animals as a cause for a lack of sexual desire. It is possible that moderate deficiencies of these hormones might exist without clinical symptoms other than reduced sexual desire. It is the opinion of the author, based on results of hormone therapy, that a hormone deficiency is not a

common cause for a lack of sexual desire in male animals.

The prognosis in reduced sexual desire or impotency is guarded to poor depending upon the cause and the degree of the inherited or acquired lack of libido. The environmental factors causing or promoting the lack of sex drive can be overcome or moderated so that libido and breeding ability can reach their maximum expression for the individual male. For males affected with a lack of libido it often requires 3 to 6 months or more of proper handling for sexual desire to noticeably improve after adverse influences have been corrected.

Treatment should only be instituted after a careful study of the male's breeding history, after a thorough physical examination of the male, and after careful and repeated observations of the male during coitus. Proper balanced and restricted amounts of good quality grain and roughage should be provided to reduce obesity, if present, or to increase body condition if the male is too thin. Sufficient exercise should be provided. Chronic disease states, especially parasitisms in young males, should be corrected or alleviated if possible. The virility and service potential of the male should be assessed and the frequency of service should be reduced, if necessary, to the male's inherent capacity. Often a period of several months of sexual rest is desirable in males that have been excessively overused. If necessary, changes should be made in the location where service occurs to assure good footing and adequate room. Proper restraint of the female, and care, consideration and patience in the handling of the "slow breeding" male may improve his sexual behavior. If the male is collected with the artificial vagina then a skilled operator should be used. The artificial vagina should be neither too warm nor too cold and adequate pressure should be applied to the penis. Some bulls prefer a coarse, heavy rubber liner to a light, smooth, thin one. A bull that is a "slow breeder" at an artificial insemination stud may benefit from a long period of sexual rest or transferring to another stud with a different group of handlers and different practices. Frequent changes of mounts and a longer period of "teasing" or stimulation is often helpful. In some instances libido may be restored by allowing the male to run loose with one or more quiet non-pregnant females in a pasture or enclosure. As a last resort when the condition fails to respond, bulls, rams and boars may be collected by electroejaculation and dogs may be collected by manual manipulation.

Treatment of impotency in male animals, especially stallions, requires a careful complete history, a complete physical examination and careful repeated observations of the male before and during the sex act under a number

of environmental and management situations and most importantly patience and understanding. This often requires a long period of sexual rest as horses have a long memory. Retraining should only take place during the regular breeding season in photoperiodic animals. Keeping discipline to a minimum during the sex act and promoting all factors that will make the sex act a pleasurable experience is essential for the "inhibited" male. The "stimulus" or mount animal should be highly attractive or desirable to the male, be quiet, the right size and strongly in estrus so it will remain immobile during the sex act.^{36,37,39,45} The use of an artificial vagina by a skilled operator has proven helpful in many impotent stallions.^{30,36} In some timid, shy, arthritic, lame or overly aggressive stallions, training them to mount a phantom or mannikin and collection with an artificial vagina has been successful,³¹ especially if an estrous mare is positioned next to the phantom. In other stallions it was necessary to permit unrestrained coitus with highly receptive mares in a paddock or pasture environment. This increases the possible risk of injury. In many instances following the recovery of the impotent stallion or male, careful, supervised and understanding breeding practices together with the use of the artificial vagina resulted in the male returning to satisfactory service. Some cases of impotency may be incurable.

Pickett and co-workers³⁶ and Rasbech³⁷ have cited a number of impotent stallions where urination occurred during about 30 percent of the ejaculations. Using a special funnel device and shortened artificial vagina the ejaculates of these stallions were fractionated and the contaminated portions were discarded.³⁶ Testicular biopsies and/or aspiration sample of the contents of the tail of the epididymis may be necessary to diagnose whether azoospermia is due to a functional, organic or degenerative condition. The latter two would occasion a very poor prognosis.

Drug and hormone treatments are of questionable value in most males lacking sex desire. Testosterone in oil or in the "Repositol" form may be used in intramuscular doses of 100 to 500 mg. in bulls and stallions, 50 to 100 mg. in boars and rams and 10 to 50 mg. in dogs and repeated every 2 to 10 days for several injections. Prolonged high level androgen therapy should be avoided because of the possibility of producing testicular degeneration and atrophy caused by the suppression of the gonadotropic hormones. One or more injections of chorionic gonadotropin at 4 to 7-day intervals in doses of 5000 to 10,000 IU for large animals and 100 to 500 IU for dogs may help stimulate testosterone production by the interstitial cells. Other forms of ICSH or LH may also be used. Males that are obese or lazy, possibly due

to a hypothyroid condition, may benefit from feeding iodinated casein with a 3 percent thyroxine potency at a rate of 1 gm. per 100 lbs. of body weight daily. Thyroxine may also be used. This helps increase the metabolic rate, hastens the loss of weight and occasionally improves the libido. Benzidine and other stimulants as well as the glucocorticoids and tranquilizers have been used with very questionable success one-half to 24 hours before breeding the impotent male. Injections of vitamins and feeding of trace minerals, protein and iodine have little value in most slow breeding males. In lame, arthritic stallions or those with laminitis, butazolidin or a similar drug may reduce pain and encourage copulation. Two stallions with failure of ejaculation apparently responded to pilocarpine and ephedrine.³⁷

Other factors such as structural lesions of the limbs and diseases of the penis and sheath may cause a reduction in libido in some males but in others can actually interfere with or prevent normal copulation. Initially males that develop an inability to mount and ejaculate may exhibit good libido, but with repeated failures, or due to painful lesions, sexual desire may become greatly reduced or lost.

Joint, Muscle, Nerve, Bone and Tendon Injuries and Pathology. Lesions affecting these structures particularly if they involve the rear quarters may cause a reduction or even cessation of mating behavior and copulation especially in males with genetically reduced virility or sex drive. Coxitis is seen most commonly in dogs as hip dysplasia and in boars, and less frequently in bulls, rams, bucks, and stallions. It is characterized by a short stride and adduction of the limb. Rupture of the round ligament may be observed in bulls with degenerative coxitis. Occasionally bulls or other males may have one or both hips dislocated resulting in inability to copulate. (See Figure 174.) Gonitis is common in bulls and is characterized by a short, stiff gait and distention and enlargement of the capsule of the stifle joint. Rupture of the anterior cruciate ligament of the stifle occurs rarely in bulls but is common in the smaller breeds of dogs. This condition in the adult bull usually prohibits mounting. Excessively straight rear limbs, resembling the Elso-heel condition described in cattle⁸ predispose bulls and stallions to injury of the stifle joint and tarsus. Gonitis, tarsitis or degenerative joint lesions (osteocondrosis) in the fetlock or phalangeal joints, or ringbone, may result in pain and reluctance or refusal to mount and copulate.

Other conditions causing similar signs of reduced libido include over-grown claws or hooves, suppurative pododermatitis, quitters or interdigital granulomas, especially in beef cattle, foot rot or interdigital necrosis,

tendonitis, suppurative arthritis of the coffin joint, laminitis or founder,⁷ traumatic injury to the peroneal nerve resulting in a "dropped" hock and "cocked" fetlock joints, myositis or muscle rupture especially involving the gastrocnemius or large gluteal or croup muscles and other traumatic lesions of the lower portions of the rear limbs. A progressive lameness resembling laminitis eventually resulting in refusal to stand, was described in related Hereford bulls and was probably caused by a recessive character.⁴ Polyarthritis may occur in swine due to erysipelas, streptococci, mycoplasma or other organisms. Occasionally polyarthritis may occur in bulls secondary to a primary site of infection. Fractures of the pelvis are rare in males.

In bulls, dogs and occasionally other males symptoms of impotency may be related to spinal disease and characterized by stiffness and soreness in gait, spinal rigidity, and pain over the vertebrae. If the spinal cord is compressed then a slight to marked paresis may be present with a swaying, unsteady gait a slightly flaccid tail and dragging of the rear limbs. Vertebral osteophytes were very common in dairy and beef bulls over six years of age with the possible exception of Brown Swiss bulls and resulted in ankylosis and spondylosis of the thoracic and lumbar vertebrae with occasionally a secondary fracture of the spine.^{2,6,9} A later study indicated that vertebral body osteophytosis were similar in bulls bred once or 6 times a week for 4 to 8 years. The influence of these osteophytes on libido in bulls were minor with only a slight increase in reaction time in bulls, with the larger lesions.¹ Synostosis of the sacroiliac joint begins at 2 to 4 years of age in the bull and is complete at 6 to 10 years of age. This is physiologic and no inflammatory signs are observed. Bulls with spondylarthroses especially of the lumbosacral joint, would mount too far caudally on the cow, exhibited lordosis and the penis was extended only a short distance and directed too far ventrally but sexual desire was good.² Bulls with spondylosis, often involving most intervertebral spaces and discs, exhibited kyphosis, a stiff back, short stiff hind leg movements or "goose stepping," and loss of liveliness and mobility. In some bulls mounting was aided by the jaw and neck of the bull pressing on the back of the cow. Spondylarthrosis affected bulls at an average age of 5 years and spondylosis was most common in older bulls, about 10 years of age. Although common dysplastic lesions in bulls might be genetically conditioned² the possibility that these conditions and arthritis might be nutritional due to excessive calcium intake was demonstrated.⁶

In dogs, especially those of the brachycephalic breeds, such as the Dachshund, prolapse of the intervertebral discs

causing compression of the spinal cord results in similar symptoms associated with an inability to copulate. Rarely tumors, such as lymphocytoma may invade the spinal canal producing compression of the spinal cord and chronic progressive paresis. Depending on the severity of the spinal cord compression, stallions with the "wobler syndrome" may or may not be able to mount and copulate. Swedish Landrace boars, especially certain sire lines, had difficulty in copulating due to bone and joint lesions or arthrosis deformans.⁵

In spastic syndrome, crampiness or "stretches" in bulls, severe acute attacks may interfere with or prevent copulation due to the prolonged spasm of the skeletal muscles of the rear limbs and back. (See Figure 175.) Spastic syndrome has been observed in all breeds of cattle but most commonly in the Holstein Friesian and Guernsey breeds. It is probably inherited as a single recessive factor with incomplete penetrance.^{3,8} It is seen most often in bulls over 3 years of age and is often associated with arthritis or painful lesions of the rear limbs. Spastic signs are not observed when the bull is lying down but become evident on standing. In most bulls the signs are mild and persist for the lifetime of the bull with occasional periods of exacerbation.

The **prognosis** for future breeding in males with joint, muscle, tendon, bone, or nerve lesions depends upon the nature and severity of the condition and the species, age and value of the animal.

The **treatment** in most cases will consist of sexual rest and restriction of activity enforced by confinement in a box stall or small paddock with good footing. In fractures of the spine, dislocation of the hips and compression of the spinal cord due to arthritic lesions and tumors in large animals, the prognosis is poor to hopeless. In arthritic lesions, the prognosis is also poor but often two to eight months or more of rest may permit limited use of the male. Improved or recovered males should be handbred where the footing is good and where the rear parts or the entire female animal are placed in a pit so the male can easily copulate, or breed an artificial vagina. In bulls or rams judicious use of an electroejaculator might permit the collection of semen from males that are unable to copulate or that might further injure themselves if allowed to mount naturally. Some males can be trained to ejaculate into an artificial vagina with all four feet on the ground. In dogs with disc lesions surgery may be indicated. In suppurative arthritis of the coffin joint prolonged conservative therapy, not amputation of the claw, is indicated so ankylosis of the joint will occur. Even if the joint is left deformed it will help the remaining normal claw support the animal's weight. Quittors or interdigital granulomas should be removed

surgically followed by stall rest and possibly wiring the toes together. In bulls with acute attacks of spastic syndrome where treatment is necessary, "Tolserol" (Squibb) or "Mephinesin" (Abbott) in 8 to 10 gm doses orally three times a day (24 to 30 gms daily) for 2 to 3 days may be administered. Tranquilizers will also help these affected bulls but the bulls should then be observed closely for the duration of the treatment to prevent injury to themselves upon rising. Glucocorticoids or butazolidin or other nonsteroidal prostaglandin antagonists for several days may also be of supportive value for the alleviation of arthritic signs. Regular hoof trimming is desirable for all large male animals. Lesser infectious or traumatic lesions should receive appropriate and prompt treatment.

Diseases of the penis and prepuce are common causes for inability or difficulty in copulating and frequently result in a marked reduction in sexual desire.

Inability to normally protrude the penis (phimosis) may be due to: (1) a congenital anomaly in the development of the penis and prepuce, with or without hypospadias, or male pseudohermaphroditism. This may be observed in all species but is seen most commonly in Boston Terriers in which the penis is very short and opens through a defective prepuce just anterior to the scrotum.⁵ Copulation is not possible. The author has observed one case of a double penis, diphallus, in a bull that prevented normal copulation because of its forked configuration. The urethra was present in only one of the two glans of the penis. (See Figure 164.) A congenital urethral opening ventral to the anus associated with two separate scrotums each containing a testis has been described in a ram.¹³

(2) A congenitally short penis has been described in bulls, bucks, boars and horses. The author and others⁴ suspect this condition may be hereditary since the latter observed it in 20 sons of a Hereford bull and the former observed it in two closely-related Guernsey bulls. The retractor penis muscle in these bulls was normal. No adhesions or lesions were present in the prepuce or around the penis preventing normal extension of the penis. As young bulls these affected males may breed heifers naturally even though only 6 to 15 cm. of the erect penis protrudes from the sheath. As the bulls get older, their abdomen gets deeper and they become less agile, copulation is impossible as the penis cannot reach the vulva of the cow. In one Guernsey bull the penis was 22 cm. shorter from the tip of the glans to the ischial arch than a penis from a similar-sized bull of the same age. These males can still be collected by an artificial vagina but their use as sires should be discouraged. The author has observed one 12-year-old stallion with a short penis the

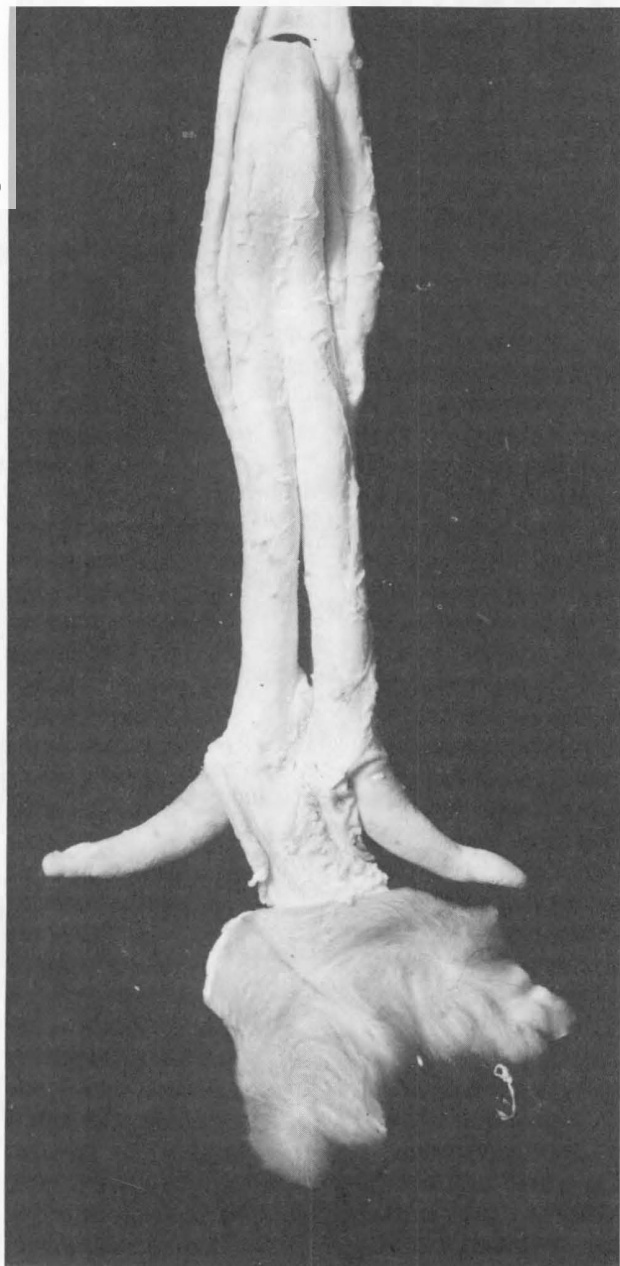


Figure 164. Diphallus in a Bull.

glans of which failed to "bell" when copulation occurred. This stallion had a normal breeding history from 5 to 10 years of age but then an inability to ejaculate on intromission developed. In bulls with a short penis the sigmoid flexure does not form a sharp S-curve in the resting state. A similar defect was described in bucks,¹⁵ and in boars.^{1,10} In the latter the pendulous, infantile,

incompletely erect penis would only extend 2 to 5 cm. beyond the preputial orifice.

(3) A congenital short retractor penis muscle was described as a probable recessive character in Friesians in Holland and symptoms were similar to those exhibited by bulls with a short penis.⁶ Myectomy of this paired muscle midway between the anus and the base of the scrotum, or removing a 4 cm. section of muscle, resulted in improvement in the ability to protrude the penis at erection in some of the affected young bulls. This operation was forbidden in the Netherlands because of the hereditary nature of this defect.¹⁶ It is possible that some of the affected young bulls failing to respond to the operation had a short penis. Ten of 38 affected bulls mated normally as young bulls and the other 28 cases were diagnosed at a young age. Of interest in regard to the above condition is the observation¹² that old bulls may have the retractor penis muscle nearly completely calcified yet copulation may be normal with a fully extended penis.¹⁰ If myectomy of the retractor muscle is performed it should be done just below the ischial arch to prevent adhesions which occurred if the operation is performed just above the sigmoid flexure of the penis.⁹ Passive stretching of the retractor penis muscle was of value in some cases.

(4) Other conditions that cause an inability to normally protrude the penis are psychic impotency,^{7,11} injury or lesions of the lumbar or sacral region,^{2,8} phimosis due to adhesions in the sigmoid flexure area of the penis or of the prepuce, stenosis of the preputial opening from congenital, traumatic or infectious causes, and tumors of the penis and sheath. Rare instances of eunuchoidism have been described^{3,17} in bulls and dogs characterized by a complete lack of sexual desire and marked hypoplasia of the genital organs and penis. This might be a congenital condition in young males or due to Sertoli cell, pituitary, or hypothalamic tumors. In three psychic infertility cases, the affected adult bulls would protrude their penis normally but then on mounting the cow the penis would be retracted before coitus.¹¹ Sexual rest and the use of an artificial vagina on one bull and resection of the retractor muscle on the other two bulls restored their ability for natural service.^{2,11} The inability of a bull and boar to obtain and maintain an erection and protrude the penis may be due to vascular shunts or anomalous venous drainage of the corpus cavernosus penis. (See Miscellaneous Causes for Inability to Copulate.)

If a bull is unable to protrude his penis normally a careful physical examination of the penis and prepuce should be made. The use of tranquilizers, pudendal nerve blocks or an electroejaculator may be helpful in arriving at an accurate diagnosis. A good history and careful observation at several attempts at natural service are very

informative. The penis should be withdrawn from the prepuce and the penis, the retractor penis muscle and the prepuce should be carefully examined. Occasionally young poorly-grown males may be slow to reach puberty and the inability to protrude the penis may be due to the normal prepuberal adhesions between the prepuce and the penis. Bulls with a short penis should be slaughtered and not used for breeding purposes because of the possible hereditary nature of the defect.

Deviation of the penis or phallocampsis is a common cause for difficulty or inability to copulate and a loss of libido. These deviations, of persistent penile frenulum, spiral or "corkscrew" glans penis, S curve or "rainbow" curve of the penis are observed most commonly in the polled, English beef breeds including the Angus, Short-horn and Hereford^{7,8,9,14,20,21} and are seldom observed in the Charolais, Brahman and dairy breeds that have a larger thicker penis. Deviations of the penis may also be due to congenital persistence of the penile frenulum in many breeds of bulls, especially Angus, and uncommonly in dogs and boars.^{1a,10,11} It was observed in six of 18 closely related, inbred, subfertile Angus bulls.⁸ The incidence of persistent penile frenulum in Angus bulls was about 1 percent with some herds having an incidence of 4 to 5 percent.⁷ The use of these bulls after treatment is questionable for genetic reasons. Two Cocker Spaniels had persistent penile frenulums.^{6,16}

A persistent frenulum is a band of tissue that extends from near the ventral tip of the glans penis to the prepuce. It is seen occasionally as a cause for a sharp ventral bending or deviation of the glans penis in bulls.^{1b} It has been reported in dogs where it caused discomfort and pain at puberty,^{12,13} and also in boars.^{1a} At birth the epithelial surfaces of bovine porcine and canine penis and sheath are fused and ventrally the penis and prepuce are united by a band of connective tissue called the frenulum. Epithelial separation and rupture of the frenulum occurs normally at puberty. When a persistence of the frenulum occurs there is usually a blood vessel present in the center of the tissue band comprising the frenulum. Cutting of the connective tissue band, without ligation, is a simple procedure and is uniformly successful for the correction of a persistent frenulum. Congenital curvature of the penile bone in the dog is rare.¹⁰

The spiral or "corkscrew" type of deviation of the penis is most commonly seen in young bulls, 2-1/2 to 5 years of age. (See Figure 165.) Many affected bulls have successfully bred cows for a year or more before the deviation is noted as a cause of infertility.^{3,7,20,21} There is evidence to indicate that this condition may be inherited as cases have been noted in sons or closely related descendants of an affected bull, especially in the polled



Figure 165. A Spiral or Corkscrew Deviation of the Penis of an Angus Bull.

beef breeds.³ In most cases of a spiral deviation, the corpus cavernosum appears longer than the supporting structures of the penis including the fibrous tunics. The anatomical basis for the spiraling of the bovine penis is well-described.²⁻⁵ When complete erection occurs the corpus cavernosum in the free end of the penis rolls inside the fibrous tunic and the penis slips and pushes laterally under the dorsal apical ligament through the less dense portion of the fibrous tunic and the glans spirals counterclockwise, ventrally and to the right around the line of the penile raphe. This may be favored by the early maturation of the supporting structures of the penis and the later maturation and growth of the penis under the continued influence of testosterone especially in the English beef breeds that have a narrow, thin penis. "Corkscrewing" of the penis occurs at the peak of erection when the integument covering the free end of the penis is stretched. If erection is only partial it does not occur. This may account for the fact that some bulls will only be observed to "cork-screw" occasionally. The author observed an affected Angus bull that was collected several times in rapid succession in an artificial vagina. On the fourth collection "corkscrewing" of the penis did not occur until after the penis entered the artificial vagina. Thus the report of Seidel and Foote^{18,19} who photographed the penis through a transparent artificial vagina at the moment of ejaculation and noted a transient twisting of the penis during more than half of the ejaculations in normal Holstein bulls is significant. Up to 30 percent of Hereford bulls have a normal straight penis on intromission but have a curled or twisted penis on dismounting.^{2,5,17} Spiralling of the penis after intromission in normal bulls may increase the tactile stimulus and promote ejaculation.⁵ In affected bulls premature full

erection occurs prior to intromission resulting in "corkscrewing" that prevents the completion of coitus. Contraction of the retractor muscles of the sheath during erection might be an additional causative factor in spiralling of the penis.² Spiralling of the glans penis is also observed in bulls being collected by the electroejaculator. Some bulls that show a spiral deviation during electroejaculation, especially if the penis is manually manipulated, may breed cows naturally without a deviation being evident.

Other less common types of deviations of the penis are the ventral or "rainbow" and the mild S-shaped curvatures which are also caused by an insufficiency of the apical ligament of the penis.^{2,6,21} The latter is of little importance and some affected bulls breed successfully. The former definitely prevents normal copulation as the more erect the penis becomes the greater the ventral curvature. A persistence of the frenulum or a short retractor penis muscle are not present. Rarely trauma and scarring of the penis and/or prepuce may cause a penile deviation.

Treatment of the spiral deviation, the ventral or "rainbow" and the S-shaped deviation usually requires a surgical operation in which either a portion of the fascia lata is implanted between the apical ligament and the tunica albuginea or the apical ligament is firmly fastened to the penile tunica albuginea.^{20,21} Various synthetic prosthetic implants have been used unsuccessfully to repair spiral or ventral deviations of the penis. Carbon fiber implants show some promise of being of value in producing a strong adhesion between the apical ligament and the tunica albuginea.¹⁵ These surgical techniques to correct a spiral or "corkscrew" curvature assist in preventing the rotation of the corpus cavernosa within the



Figure 166. Ventral or "Rainbow" Deviation of the penis of a Hereford Bull.

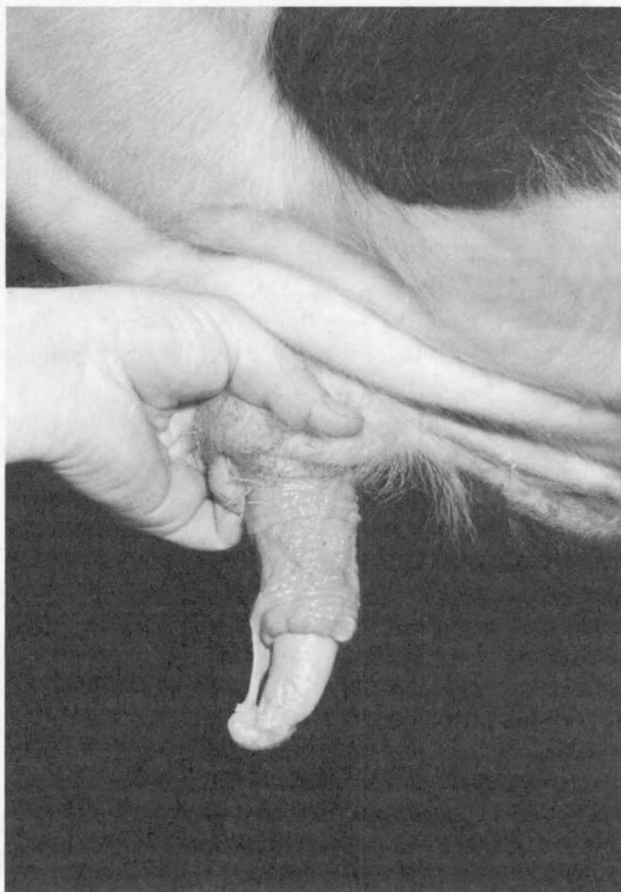


Figure 167. A Persistent Frenulum, a Cause of Deviation of the Bovine Penis.

fibrous tunic by producing adhesions between the two structures.

Hematomas, Adhesions of the Penis and Prepuce, Tumors, Phimosis and Paraphimosis—Decreased libido and inability to copulate may be associated with phimosis of the penis due to adhesions of the sigmoid flexure of the penis or the deeper portions of the prepuce, tumors of the penis and prepuce, stenosis of the preputial orifice, paraphimosis or paralysis of the penis or a stenosed preputial ring.

1. **Adhesions of the penis in the region of the sigmoid flexure** in bulls and rams may be due to trauma from horn injuries or in bulls from injections of local anesthetics to block the dorsal nerve of the penis as was earlier performed to produce anesthesia of the penis to aid withdrawal from the sheath. These connective tissue adhesions prevent obliteration of the S-curve and penile protrusion at the time of erection. Treatment to relieve

these adhesions often results in more severe adhesions.

Adhesions of the deeper or caudal portions of the freely-moveable prepuce to the abdominal wall or to the skin in the region of the fornix produces a more severe phimosis than adhesions of the cranial portion of the prepuce. These adhesions may be secondary to lacerations of the prepuce especially in young bulls where the prepuce has not yet completely separated from the glans, or in older vigorous bulls, especially those used in artificial breeding studs and collected with artificial vagina, in which a vigorous thrust may tear the prepuce away from its attachment to the glans for one-third to the entire circumference of the penis. Infection that follows this injury may produce abscesses and/or adhesions to the surrounding structures preventing the free movement of the prepuce and penis at erection. (See Figures 168 and 169.) Prompt antibiotic therapy both locally in an oily base and parenterally for 7 to 14 days is recommended together with sexual rest for 6 to 12 weeks. Suturing of the prepuce to the mucous membrane of the glans and the underlying connective tissue appears indicated but permitting healing by second intention without suturing has proven more satisfactory for the author.

A ruptured, "fractured," or "broken" penis with a secondary hematoma is usually observed in the bull but in rare instances may occur in the stallion due to the mare's kicking the erect penis as the stallion mounts. In the dog, fracture of the penile bone may be caused by a traumatic injury and may require amputation of the penis or resection or removal of the penile bone.¹² Similar traumatic injuries in the other species are uncommon. In the bull, the condition of a "fractured," "broken," or ruptured penis occurs most commonly in active bulls



Figure 168. Tearing of the Prepuce from its Attachment to the Glans Penis in a Bull.



Figure 169. A Chronic Abscess Causing a Severe Phimosis in a Bull. (This abscess was probably secondary to a laceration of the prepuce or a small hematoma or "fracture" of the penis.)

with a strong sex drive breeding cows on pasture. It is rarely observed in dairy bulls that are hand bred. The injury apparently occurs at coitus either when the cow or heifer suddenly goes down under the weight of the bull, or due to a sudden ventral bending of the erect penis against the escutcheon of the cow at the moment the bull thrusts, causing a dorsal rupture of the tunica albuginea usually near the distal portion of the sigmoid flexure and opposite the initial attachment of the retractor penis muscle. Penile hematomas are apparently due to a sudden angulation or bending of the erect penis at service. They are not only due to a high blood pressure in the corpus cavernosum. Pressures of more than 10,000 mm. of Hg may occur in the corpus cavernosum penis at coitus.^{2,8,25}

Rupture of the penis usually occurs in 2- to 4-year-old bulls and is seen most commonly in Herefords. The symptoms of the injury include a shortening of the stride, stiffness, pain and a slight arching of the back that are generally mild and may not immediately prevent subsequent copulations which produce a larger hematoma. A swelling rapidly develops just cranial to the scrotum that varies in size depending upon the amount of hemorrhage from the ruptured penis and the tissues involved.^{16,17} Hemorrhage is profuse and in a "hand grenade" effect because of the very high blood pressure present in the erect corpus cavernosum penis. Prolapse of the prepuce may occur secondary to the edema that often develops. There is usually no difficulty in urination. At first the swelling is soft and fluctuating; later it becomes firm as the hematoma clots and organizes. Pain may be evident but heat is slight. Systemic symptoms are usually lacking. The bull shows definite reluctance and inability to copulate. If treatment is not undertaken

the clot organizes. The hematoma may become infected producing an abscess. (See Figure 169.) Adhesions may occur between the prepuce, penis, abdominal wall and skin rendering the bull useless for future service. A differential diagnosis from other conditions such as tumors, chronic fibrous adhesions, lacerations of the penis and prepuce and rupture of the urethra should be considered.

The prognosis in these cases should be guarded even when an operation is performed. If an aseptic surgical operation cannot be performed an operation should not be attempted. In this latter situation the bull should be given large doses of parenteral antibiotics for one to two weeks to prevent abscessation. About 50 percent of bulls may recover spontaneously with 3 months of sexual rest. Due to the high rate of recurrence and other complications, surgery is usually recommended for valuable bulls.²⁵ Hematomas that become infected seldom respond to treatment and surgery. The size of the lesion rather than its location was of greatest importance in the prognosis.^{24,25} Some affected bulls damage the dorsal nerve of the penis at the time of the "rupture" so they lose sensation in the glans. Therefore upon recovery these bulls can't find the vulva and achieve intromission and ejaculation. Before surgery the penis should be withdrawn from the sheath. If the penis can be extended completely or up to 6 to 8 inches and sensation is present in the glans the prognosis is good and surgery may not be necessary.^{16,17} If the penis can only be extended 2 to 4 inches the prognosis is guarded and if the penis can't be withdrawn from the prepuce and/or the glans lacks sensory innervation, the prognosis is poor.^{16,17} Nearly 50 percent of the hematomas not operated upon and untreated become infected by the second week after the injury.^{20,25} If abscesses are present, they should be drained and allowed to heal before surgery is performed. Conditions requiring surgery to remove extensive adhesions, abscesses, and scar tissue have a poor prognosis.

The operation commonly undertaken to correct this condition of a ruptured penis and hematoma should not be performed until after the blood in the hematoma has clotted firmly and before organization of the clot occurs. This is usually between the fourth and seventh days after the rupture has occurred. Surgery may be attempted after the third week following the injury but is contraindicated between 10 and 21 days.²⁵ From the time of the occurrence of the hematoma until the time of the operation the bull should be given parenteral antibiotics. Prior to surgery the electroejaculator may be used to determine if normal engorgement of the penis occurs and if sensation is present in the glans penis.^{24,25} If normal engorgement of the penis does not occur, an intrapenile hematoma preventing normal distention of the distal por-

tions of the corpus cavernosum is probably present. If either of these two conditions is present the prognosis is poor.

To perform this operation the bull should be restrained in lateral recumbency after the administration of a pre-anesthetic tranquilizer and gas anesthesia or chloral hydrate^{17,25} or after a large dose of epidural anesthesia (40 to 60 cc of a 2-percent procaine or xylocaine solution) together with a narcotic dose of chloral hydrate, if necessary. This latter method of anesthesia is supplemented by local anesthesia under the skin at the operative site. The operation should be under favorable conditions with as close an approach to an approach to aseptic surgery as possible, since second-intention healing produces many adhesions. After shaving and disinfecting the operative site, an oblique incision 6 to 10 inches long is made through the skin over the swelling.²⁵ All bleeding must be controlled. The clotted blood in the hematoma is carefully removed and the penis brought to the incision. The fibrin is removed. The break in the tunica albuginea is thoroughly exposed, using great care not to injure the dorsal nerve of the penis, coagulated blood in the corpus cavernosum is expressed, and the rent in the tunica albuginea which is usually 2 to 4 cm. long, spiral, oblique, or longitudinal in direction, is sutured with No. 2 chromic catgut with a shoelace stitch. Most ruptures are in the dorsal or dorso-lateral portion of the penis just cranial to the terminal curve of the sigmoid flexure and opposite the attachment of the retractor penis muscle. Following complete control of hemorrhage, the cavity may be flushed with an antibiotic or saline solution. The elastic layer of fascia containing the vessels and nerves is carefully replaced and sutured. The subcutaneous tissues are approximated with catgut and the skin closed with nylon sutures. The wound should heal by primary intention. Following the operation, parenteral antibiotic therapy is continued. Suturing the tunica albuginea is necessary to prevent a possible venous shunt between the corpus cavernosum penis and the dorsal veins of the penis.²⁵

Copulation should not be permitted for at least 2 weeks and preferably longer, 4 to 8 weeks.^{5,15,16,17,25,26} Success in preventing the development of firm adhesions around the penis was reported by keeping the bull sexually stimulated. Housing it next to a heifer or cow in estrum or teasing the bull daily was recommended. Extending the penis several times a week under tranquilization was recommended.¹⁶ Using the electroejaculator was not recommended¹⁷ until healing had taken place. Daily massage of the affected area for 10 to 20 minutes to break down adhesions and prevent new ones was also recommended.¹¹ This should be continued for 2 to 3 months.

Conservative treatment resulted in recovery in 37 of 47 cases.¹¹ Complications of penile rupture include abscess formation, adhesions preventing protrusion, analgesia of the penis due to injury to the dorsal nerves, a recurrence of the hematoma or a shunt between the corpus cavernosum penis and the dorsal vessels of the penis or the corpus spongiosum on erection.²⁵

Chronic abscesses secondary to hematomas or perforating injuries to the prepuce should be drained into the prepuce if possible to prevent adhesions between the prepuce and skin that occur when abscesses are drained through skin incisions. (See Figure 169.) If the abscess heals but adhesions preventing normal function of the penis and prepuce remain, then the bull may be operated on as described above to separate the adhesions of the prepuce and the penis from the skin or abdominal wall. The prognosis is guarded to poor.

2. Tumors of the penis and prepuce in bulls, stallions, boars and dogs may cause phimosis or paraphimosis or prevent normal intromission. In bulls the only significant tumor is the **transmissible fibropapilloma**.^{9,14} (See Figure 170.) There is definite evidence that this tumor and cutaneous papillomas, or warts (*verruca vulgaris*) in cattle are similar and caused by the same agent. It is probably infectious in nature and the etiologic agent is considered to be a virus. The fibropapillomas are similar to those observed on the vulva of heifers. They are single or multiple, firm, cauliflower-like growths. Young, susceptible bulls, 9 to 18 months of age, are most commonly affected with papillomas. Young bulls housed together frequently mount each other and may injure the prepuce, affording an invasion site for the tumor virus. Injury to the penis is also predisposed by breeding the young bull before the prepuce and glans

penis are fully separated. For these reasons young beef bulls are most commonly affected. Hemorrhage from the sheath after service and hesitancy or refusal to copulate are frequently noted in bulls with penile tumors. In boars a virus-induced papilloma of the penis which is venereally transmitted has been described.^{9,14}

In stallions tumors of the penis are uncommon and when present are usually **squamous cell carcinomas** of low malignancy. (See Figure 171.) Benign squamous papillomas, angiomas and melanomas may occur in or on the sheath and penis of horses.^{6,9} Carcinomas often ulcerate and usually bleed at the time of service and produce a fetid preputial discharge. They should be differentiated from granulomas caused by *Habronema* larvae. Squamous cell carcinomas may be favored in the stallion, bull and dog by the smegma in the sheath.⁹

The **transmissible venereal tumor** is the most common one seen in the penis and prepuce of dogs. It is usually spread by coitus. In rare instances the disease may be spread by licking of the vulvar or preputial discharges of affected dogs. Intact cells must be transplanted to transmit the tumor; it is not transmissible by filtrates. The incubation period is from 5 to 6 weeks. All breeds of dogs are susceptible. It is characterized by a discharge of a bloody, fetid exudate from the vagina of the female and from the prepuce of the male. When the penis is exposed, greyish-red nodular growths are observed on the penis and the prepuce. The tumor masses are friable and bleed when handled. In advanced cases the tumor may also be observed involving the inguinal lymph glands. The tumor ulcerates easily. It may be found in other cutaneous sites but internal or metastatic involvement is uncommon.^{9,10,14} The transmissible venereal tumor has been reported widespread throughout the

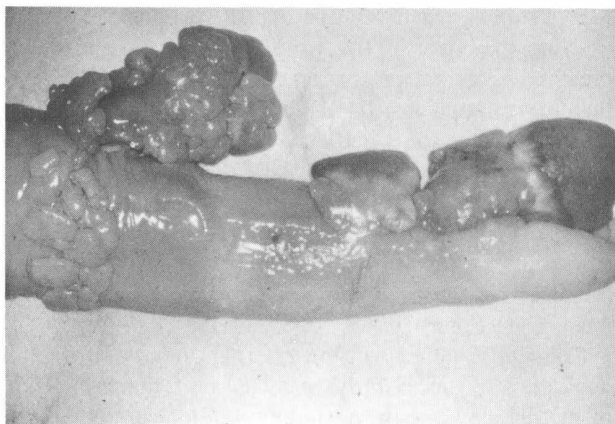


Figure 170. Transmissible Fibropapilloma of the Penis in a Young Bull. (Courtesy K. McEntee.)



Figure 171. Squamous Cell Carcinoma of the Penis and Sheath in a Stallion.

world but most commonly in tropical countries. The disease may be common in an area and then in the next decade or two disappear or be rarely observed. Papillomas, squamous cell carcinomas, sarcomas, and other tumors may occur in the sheath or on the penis of dogs.³ Recent reports have indicated that removal of the canine venereal tumors by electrocautery or surgery followed by chemotherapy with vincristine¹³ or by vincristine alone, 0.025 mg/kg. IV, once weekly for about 4 weeks⁴ appear promising. However spontaneous regression of tumors is frequent and may occur within 2 months.⁹ Tumors of the sheath and penis of rams, bucks and toms are rare.

In the treatment of penile tumors in the bull it should be noted that spontaneous recovery from infectious fibropapillomas usually occurred in an average time of less than 4 months, range 1 to 15 months.^{1,14,19} The nearer the bull was to 2 years of age the better the prognosis.⁷ If the tumors are multiple on the penis, treatment may be difficult and some veterinarians have empirically recommended the use of wart vaccine. The tissue vaccine was more effective in producing an immunity than was the egg-yolk vaccine.¹ Formalin-killed vaccine given intradermally to calves at 2 weeks to 6 months of age provided good protection.¹⁹ The vaccine was of questionable value in affected bulls. They recommended that semen from affected bulls not be used or frozen because of the danger of transmitting the virus to cows. Disappearance of penile tumors in 4 out of 5 young bulls was reported after the administration of an autogenous vaccine.²¹ However, others¹⁹ found the vaccine induced no appreciable regression in experimentally induced warts. The value of wart vaccine in the treatment of cutaneous papillomatosis is questionable on the basis of their work, which indicated fairly rapid spontaneous recoveries. Fibropapillomas have been removed by the author and others²³ from the penis of bulls when they had a narrow base or were pedunculated, by grasping and pulling them off as the bull mounts a cow. Some bleeding occurred, but it was not excessive. By means of a pudendal block or tranquilizers and local anesthesia the penis can be withdrawn from the sheath and the tumors removed with scissors or by cautery and the mucous membrane of the penis or prepuce sutured with fine catgut. The prognosis is good whatever treatment is used.

In the stallion the occasional squamous cell carcinoma can be removed by a liberal incision or if necessary by amputation of the penis. Castration should be performed prior to amputation of the penis, since both operations performed simultaneously might cause excessive tissue reaction and swelling. The operation for amputation of the penis is a standard one described by Williams and

modified by other authors,^{22,25,27} to prevent a future stricture of the urethral orifice. After restraining the animal in lateral recumbency and giving general or local anesthesia, the penis is withdrawn and thoroughly washed and prepared for surgery. A catheter is introduced into the urethra. To control hemorrhage, an elastic ligature is placed tightly around the proximal end of the extended penis. In the prolapsed equine penis the operative site is just distal to the internal preputial ring. A triangular incision is made over the urethra with the base of the triangle cranial and under the amputation site. The urethra is opened and sutured to the edges of this triangular incision. The penis is cut off at the base of the triangle. By using strong nylon sutures, the urethral wall, the ventral and dorsal portions of the tunica albuginea, and the dorsal skin of the penis, or the prepuce, but not the corpus cavernosa are drawn firmly together with many interrupted sutures, to control hemorrhage.

In the dog, surgery may be indicated for the removal of the transmissible venereal tumor. The earlier surgery is undertaken, the better the likelihood of a successful operation. Liberal excision of the involved tissue is desirable. Complete removal of the penis and prepuce is questionable as even in advanced cases the tumor may regress spontaneously. Dogs which recovered were immune.³ Whole-blood transfusions from an immune dog resulted in a cure or regression of the tumor in affected dogs. In severe cases where it is difficult or impossible to remove all of the involved tissue, radiation therapy may prove of value. Claims for cures of this disease in dogs should be considered with caution because of the high incidence of spontaneous regression usually occurring in less than six months.³ Spaying of females and elimination of stray dogs is very helpful in controlling the disease.¹⁰

3. Phimosis or stenosis of the preputial orifice, chronic prolapse of the prepuce, and paraphimosis preventing normal protrusion of the penis is a cause of inability to copulate. It may occasionally be congenital in young dogs, toms and stallions. Stenosis of the preputial orifice is usually acquired due to injuries, wounds and infections. In cattle with pendulous sheaths, the preputial orifice may be stepped on causing severe contusion and swelling. In beef bulls chronic prolapse of the prepuce is a very common cause of posthitis and phimosis (See Figure 172.)

Congenital stenosis of the external preputial orifice in dogs may be successfully corrected by a dorsal incision of the orifice. Incising a stenotic internal preputial ring in a stallion to permit normal erection and protrusion of the penis was described.⁴ Removal of the preputial ring in a young cat with dysuria and paraphimosis was re-



Figure 172. Chronic Prolapse and Stenosis of the Preputial Orifice of a Santa Gertrudis Bull.

ported.⁶ In the bull, dog or ram the usual procedure to correct a simple stenosis of the preputial orifice caused by cicatricial tissue is to remove from the ventral of the sheath a triangular portion of skin. The base of the triangle is at the preputial orifice. After the skin is removed an incision is made through the midline of the prepuce to the apex of the triangle and after careful hemostasis the preputial membrane is sutured to the skin by interrupted catgut sutures.

Chronic prolapse of the prepuce is most common in **Bos indicus** cattle such as: Santa Gertrudis, Brahman or Zebu, or their crosses, in **Bos taurus** cattle it is less common but is seen in the polled beef breeds such as: Angus and Polled Hereford cattle. It is occasionally seen in other beef breeds and is rare in dairy cattle. It probably is an inherited trait. (See Figure 172.) In Polled English breeds prolapse of the prepuce may be due to a genetic absence of the retractor muscles of the prepuce.¹¹ In these breeds the circumference of the preputial orifice and the length of the prepuce was similar to the normal breeds. In the affected breeds the prepuce commonly prolapses 7 to 20 cm. and depending on the nature of the grazing area, especially the height and type of brush or herbage, and time of year, the prolapsed sheath becomes dry, traumatized, lacerated, frost-bitten, edematous, swollen and fibrotic. Screwworm infestation may also occur resulting in phimosis and rarely paraphimosis.

In mild cases diagnosed early the affected bull may be confined in a well-bedded stall. The prolapsed organ should be carefully washed, cleansed and dried. Oily antibiotic or bland antiseptic preparations are applied and the prolapse replaced and held in place by a purse-string suture around the preputial orifice. Repeated treatments

two to three times a week for three to four weeks before allowing breeding are indicated. In more severe cases where replacement is not possible, circumcision or even amputation of the affected portion of the prepuce may be necessary.

Before surgery in severe cases the sheath and penis should be cleaned with hydrogen peroxide and furacin solution, and oily antiseptics or antibiotics and lanolin be applied for about a week to the prolapsed structures under a stockinette held in place by a rubber band.^{8,18} The pendulous sheath and prolapsed membranes should be supported for this period to possibly control or reduce the swelling and edema. Hydrotherapy consisting of spraying the prolapsed sheath with warm water at frequent periods daily may be helpful. Systemic administration of antibiotics and diuretics may be indicated. Other authors suggested that immediate circumcision was more practical and economical.^{2,5} In any surgical procedure as much of the prepuce should be conserved as possible. Removal of large portions of the prepuce may result in inability to protrude the penis the necessary length for natural service. In all severe preputial lesions requiring surgery or extensive treatment, a long recovery period of 30 to 90 days is required for complete healing before service should be permitted. Depending on the type and degree of prolapse of the prepuce, the breed and value of the bull and the operator's experience one of three (3) general operative procedures may be employed.¹⁸ a) **circumcision** may be employed to correct chronic prolapse of the prepuce.^{10,13,16,17,18} In Brahman bulls the prepuce is usually long enough to permit a removal of a portion of it by circumcision without causing limitations on penile extension during erection. In the English breeds the operator must conserve as much preputial membrane as possible so the reefing or resection^{8,15,18} operation is preferred. Following tranquilization and restraint in lateral recumbency the prolapsed tissues are washed, cleansed and anesthetized.^{8,18} General anesthesia may be used. An inverted triangular incision, 5 to 7 cm., 2 to 3 inches, on a side is made on the ventral, posterior aspect of the sheath through the skin only. The base of the triangle is at the preputial orifice. After removal of the skin an incision is made through the ventral caudal midline of the prepuce to the apex of the triangle. Careful hemostasis is highly essential before placing interrupted nonabsorbable nylon sutures to secure the internal preputial membrane to the skin. This later prevents the possibility of scarring and stenosis of the preputial orifice. Then the diseased prolapsed portion of the prepuce is removed after placing interrupted nylon sutures around its circumference firmly securing the internal preputial membrane to the external at the preputial orifice. These

sutures are usually about 4 cm. apart on the outside and 1.5 cm. apart on the inside. They should be drawn tightly and overlap to completely control hemorrhage then the prolapsed portion of the prepuce is removed about 1 cm. distal to the suture line. Following the operation the sheath should be supported against the body wall for two weeks.

The sutures can be removed in about 6 to 8 days. Parenteral antibiotics should be given for 7 to 10 days. b) **"reefing" type of operation** involving resection and anastomosis is superior to other procedures, particularly when the midportion of the prepuce is involved, or when as much prepuce as possible must be conserved.^{8,15,18} An incision is made at the skin line of the preputial orifice and at the distal end of the prolapse where the "inner" preputial membrane is normal. A longitudinal incision is made between these two initial transverse incisions and the diseased "outer" preputial membrane and underlying edematous, fibrous or abscessed tissue is removed. Hemorrhage must be carefully controlled. Electrocautery, maybe a useful adjunct to ligatures. The normal preputial membrane and underlying tissue is sutured carefully by many interrupted catgut sutures to the skin and subcutaneous tissue at the preputial orifice.^{2,5,8,15,17,18} Antibiotics should be administered locally and systemically for the next 7 to 10 days. A large Penrose drain fastened into the sheath and around the penis to prevent irritation of the suture line by urine and a purse-string suture in the skin at the orifice to invert the suture line was recommended.¹⁵⁻¹⁸ This purse-string suture is removed after one week. If following this treatment constriction of the preputial orifice occurs then a second operation consisting of a triangular-shaped incision on the ventral-caudal aspect of the preputial orifice is performed as previously described. As a preventive measure in bulls affected with chronic prolapse of the prepuce, removing a large-V-shaped wedge of skin from the suspensory skin flap of the sheath to reduce its pendulous attachment has been suggested.^{1a}

Where the prepuce is more extensively involved some veterinarians¹⁸ use an c) easier amputation technique where the entire prolapsed part is removed by through and through overlapping sutures over a perforated plastic ring securely fastened by interlocking sutures into the preputial orifice. This may result in too great a loss of normal preputial membrane.

Bulls with a lack of libido and sex drive may fail to breed satisfactorily after these treatments because of pain associated with erection and coitus. Chronic prolapse of the prepuce may be prevented or controlled by the selection of bulls with smaller preputial orifices and with less tendency to prolapse their preputial membrane. It is questionable and probably undesirable to operate on af-

fected bulls since this condition is genetically predisposed. These bulls should be culled to decrease the frequency of this trait in the population. Males should be selected for lighter, less pendulous sheaths with smaller preputial orifices and stronger retractor penis muscles.^{7,14} Surgical procedures for prolapse of the penis and prepuce in boars and dogs has been described.^{1a,c}

Paraphimosis, the inability to withdraw the penis into the prepuce, results in edema, swelling, and balanoposthitis. It may occur following erection of the penis through a stenotic preputial ring or orifice caused by a congenital or acquired stricture or by tumors as noted above under phimosis. Paralysis of the penis and paraphimosis may be due to spinal disease or trauma. Paralysis of the penis is seen in bulls with rabies and in horses in the late stages of dourine. It is possible that the posterior paresis reported in a few cases of rhinopneumonitis, due to equine herpesvirus 1, might be the cause of occasional unexplained cases of penile paralysis in stallions. Resection of the retractor penis muscle in bulls with pendant sheaths may cause paraphimosis. It is not observed in the dairy breeds with a sheath that is closely attached to the abdominal wall. The author has observed and had reported to him at least 15 cases of paralysis of the penis with paraphimosis in geldings and stallions following the use of phenothiazine-derived tranquilizers. The product most commonly associated with prolonged or permanent paraphimosis has been withdrawn from the commercial market.

The prognosis in paraphimosis in males is guarded and depends upon the promptness of treatment and the degree of trauma or necrosis present. Support of the prolapsed penis and sheath is essential to minimize gravitational edema.^{13,18} Cases of paraphimosis in horses following castration and the use of tranquilizers should have the penis supported or held within the sheath within an hour or two of its occurrence to prevent a chronic prolapse of the organ often necessitating amputation. Cold packs and pressure may reduce the swollen penis and allow replacement. In some cases in dogs and occasionally in bulls, enlargement of the preputial opening is necessary in order to replace the penis and prevent a recurrence of the condition. For necrosis of the penis secondary to acute paraphimosis and for chronic paralysis and prolapse of the penis in dogs and cats is amputation is recommended. To correct chronic protrusion of the tip of the canine penis due to a "short" prepuce, a "long" penis or inefficient cranial preputial muscles surgically shortening these muscles or removing an elliptical portion of skin cranial to the prepuce to draw the prepuce over the penile tip is recommended.^{3,6a,b,9}

In bulls cleaning of the penis, removal of necrotic tis-

sue, and the liberal application of ointment was recommended.¹⁷ Gauze should be wrapped around the penis to protect it. The penis with its gauze dressing should be placed inside the sheath as soon as possible. Petroleum jelly should be packed into the sheath to prevent adhesions. Frequent withdrawal of the penis and applications of ointment are indicated.

Balanoposthitis due to infectious or noninfectious causes may produce a stenosis of the preputial orifice, adhesions of the penis and prepuce to each other or to the surrounding tissues or produce sufficient pain and discomfort that copulation is impossible or not attempted. Balanitis is an inflammation of the glans penis, and posthitis is an inflammation of the prepuce. They are often both involved in an inflammatory reaction because of their close apposition. Balanoposthitis is common in the bull, ram and dog and uncommon in the boar and cat. It is observed occasionally in the stallion.

The preputial cavity in the bull may normally contain a wide variety of bacteria, molds, protozoa and viruses including: *Campylobacter fetus venerealis*, *E. coli*, streptococci, staphylococci, *B. pyocyaneus*, *Pseudomonas aeruginosa*, *C. pyogenes*, *Proteus*, *Actinomyces necrophorus*, actinobacilli, molds (*Aspergillus*, *Mucor*, *Absidia*), mycoplasmas, ureaplasmas, *Klebsiella*, *Hemophilus*, *Trichomonas fetus*, **IBR-IPV virus**, and other pathogenic and saprophytic organisms.

Other male animals have a similar variety of infectious agents as inhabitants of the prepuce. It is often difficult to recover specific slow-growing pathogens from the prepuce of bulls and other males because rapid-growing contaminants overgrow the cultures. Granular venereal "disease" lesions or hypertrophy of lymphoid nodules on the penis and prepuce of bulls and dogs are common, but are not associated with any specific organism and have little significance. (See Figure 173.) Sexual rest and protective antibiotic solutions in oil infused into the sheath usually alleviate acute signs of granular venereal disease or mild balanoposthitis. No obvious balanoposthitis generally accompanies the presence of the above organisms in the preputial cavity with the possible exception of **M. tuberculosis** and the acute form of IBR-IPV virus infections.

Tuberculosis of the sheath, penis, prepuce, and penile lymph glands of bulls has been described.³⁷ This avenue of invasion in the bull is invited by tuberculosis of the female genital tract. Tuberculosis of the sheath and penis may be characterized by enlarged, granulomatous bleeding lesions of the glans penis, adhesions of the penis, prepuce, and sigmoid flexure with secondary phimosis. The penile lymph glands are enlarged and are likely to be abscessed. In suspicious cases either culture of the



Figure 173. Chronic Granular Venereal Disease Lesions of the Bovine Penis and Sheath.

lesions or a tuberculin test will probably establish the diagnosis. This type of tuberculosis has not been reported in recent years in the United States. Several rare cases of actinomycosis affecting the sheath and glans penis of bulls have been reported.³⁷ The lesions resembled those of tuberculosis.

Trauma, abrasions, lacerations of the prepuce or glans penis usually result in the introduction of the above wound-infection organisms into the deeper tissues with resulting swelling, inflammation, pain and preputial discharge. This is observed most commonly in young bulls especially those in which the glans penis is not completely separated from the sheath. In artificial insemination studs injuries from the artificial vagina may occur including the loss of a rubber band from the vagina onto the glans penis. This may cause a deep laceration or amputation of the glans. Young bulls running together in the early spring months may, by their homosexual behavior and frequent mounting, draw hair into their prepuce where it forms a stenotic ring at the base of the glans with an associated balanoposthitis. In rare cases this ring of hair may result in the sloughing or amputation of the glans penis. Mild balanitis and posthitis have been observed in virgin bulls or in young bulls after they have bred older cows. *C. pyogenes*, *E. coli*, and other organisms present in the prepuce of certain bulls may cause a temporary vulvovaginitis in females after coitus.³ Although many miscellaneous organisms may be introduced into the prepuce, recovery is usually spontaneous with no clinical lesions.

The herpesvirus of cattle, IBR-IPV, can produce an

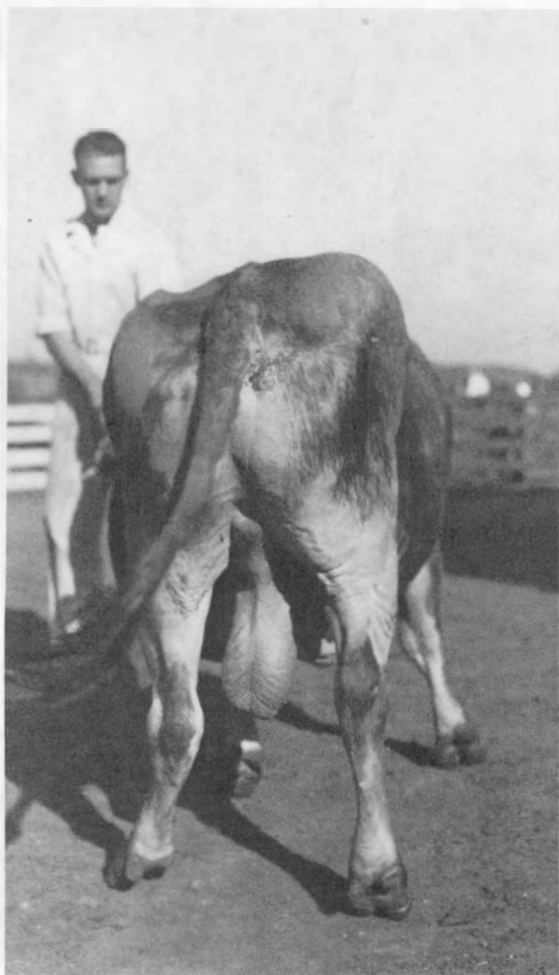


Figure 174. Dislocated Hip in a Jersey Bull.

acute inflammation and ulceration of the penis and prepuce (infectious pustular balanoposthitis (IPBP)) accompanied by a short period of elevated body temperature when introduced into the preputial cavity of susceptible bulls.^{7,26,34} This disease was formerly called vesicular venereal disease in the U.S. or Blaschennausschlag in Germany. The initial area of involvement is the epithelium over the lymphoid follicles that becomes necrotic and sloughs. The ulcers on the glans and prepuce caused by the virus are secondarily infected by the bacterial flora of the sheath resulting in a severe pustular balanoposthitis. Abrasions of the penis and sheath that occur at copulation make the lesions in the acute stage more severe. The virus can usually be recovered from the acutely affected bull's prepuce and penis for about 10 to 14 days. Bulls may spread this disease during this period to cows by copulation producing pustular vulvo-vaginitis. Some

cases of balanoposthitis may be so mild that infection may go undetected. The recovery of this virus from the prepuce of bulls for a period of up to 361 days has been reported.²⁹ These are often refractory or immune animals. Serum antibodies are developed but the titers are low 1:10 to 1:100 on the serum neutralization test.²⁵ On histologic section of affected tissues eosinophilic nuclear inclusion bodies may be found in many cells. Epizootic outbreaks of balanoposthitis in young range bulls might be due to this agent.¹¹ Lymphoid follicular hyperplasia was noted in the prepuce and penis following outbreaks of infectious pustular balanoposthitis (IBR-IPV) in bulls.^{19b} A few outbreaks have been reported in artificial breeding studs where there is a great danger of this virus being disseminated in liquid or frozen semen since antibiotics commonly placed in semen extenders have no effect on this virus.²⁵ Coital exanthema due to the IPV virus was common in dairy herds and was occasionally seen in AI centers in Germany.³² It was demonstrated by electrophoresis that the IPV virus differed from the IBR virus even though by serological methods they were similar.³³ A highly attenuated vaccine was prepared that would protect the cows and bulls if instilled intranasally and intravaginally or into the prepuce of bulls yet would not produce signs of the disease even if semen from recently vaccinated bulls was used for artificial insemination. The field strain of IPV virus if present in the semen would reduce conception rates by about 7 percent and produce signs of the disease. This highly attenuated vaccine was administered as noted above twice at 6-week intervals and then once yearly thereafter. No abortions were produced by the vaccine given to pregnant cows and challenged cattle showed no evidence of disease. The local immunity produced by this vaccine was better than the immunity produced by an intramuscular injection of a vaccine. Bulls in one large AI stud in the U.S. are rou-

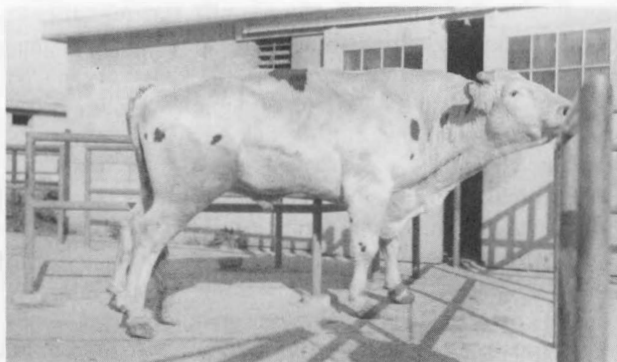


Figure 175. Spastic Syndrome or Stretches in an 8-year-old Holstein Bull.

tinely vaccinated with an IBR vaccine intranasally twice or three times a year. There is no evidence that bulls vaccinated with this vaccine have transmitted the IBR-IPV virus in the semen. This has been determined by routine cultures of over 70,000 ejaculates.^{15,26}

In severe cases acute swelling, pain and later local scarring may cause difficulty or slowness in copulation. True adhesions were not observed.^{7,34} In range bulls with great libido repeated abrasion of infected and inflamed tissues might occasionally produce adhesions. For treatment sexual rest is recommended together with local antibiotic therapy of the sheath. Most bulls recover within one to two weeks but it may take up to a month before normal copulation will occur. Because of the infectious nature of this disease bulls should not be used for service until 6 to 8 weeks after the onset of the attack. Since herpes viruses tend to persist in the body, recurrent dissemination of virus may occasionally be possible.^{25,29}

Balanoposthitis in rams, "pizzle rot" or "sheath rot," may be infectious or noninfectious. The most common infectious form of balanoposthitis is due to the virus that causes ulcerative dermatosis (lip and leg ulceration or necrotic venereal disease). This disease has been described in the U.S., England, France and Germany.^{17,20} The lesions on the preputial orifice, prepuce and glans penis are ulcerative and covered by a scab. Removal of the scab reveals a shallow, raw, bleeding crater containing a creamy odorless pus. The preputial lesions may cause phimosis or paraphimosis, and an extensive penile lesion may render the ram useless as a breeder. Lesions may also be present on the lip, nostril, feet, or vulva. The disease should be distinguished from contagious ecthyma and common non-specific lesions occasionally seen on the preputial orifice of rams. Ulcerative dermatosis is spread by venereal contact and other means. The disease in rams may persist for weeks or months. Affected rams should not be used for breeding. There is no vaccine available nor is there any specific treatment for the lesions.

Noninfectious balanoposthitis has been described in the U.S. and Australia. Two types of lesions are recognized, an ulceration of the prepuce near the preputial orifice and a stenosis of the orifice with a secondary chronic ulceration of the deeper portions of the prepuce accompanied by an accumulation of pus and necrotic material. This occurs mainly in wethers, sheep and goats, or occasionally rams 2 to 4 years of age. It is often associated with a wet spring and pasturing sheep on lush fertilized grass, rye, clover or lucerne pastures that are high in protein and the presence of a urea-hydrolyzing *C. renale* in the wether's sheath. The urine degradation products are more irritating to sheath tissue than normal

urine.^{22,28} The preputial orifice and prepuce may be ulcerated and scarred so urination is difficult. Changing of the diet to dry feed with a lower protein intake, or fasting, results in an improvement of the balanoposthitis. Young rams housed together may develop similar lesions possibly due to trauma and contamination. In severe cases the sheath may have to be surgically opened ventrally to permit urination to save the life of the animal. Extending the preputial incision too far caudally may render a ram useless for service. Superficial external lesions may be treated by proper local therapy.

A clinically similar type of posthitis was observed in many young beef bulls, but not steers, in South America and Australia. A high incidence occurred in bulls on high planes of nutrition possibly due to the presence of *C. renale* in the sheath that hydrolyzed urea to ammonia that caused the lesions. The clinical history and histologic examination indicated the condition was not due to the IBR-IPV virus. Further studies are indicated.²⁴

Balanoposthitis in the horse may occur in geldings or stallions. A thick, fibrous, fatty or edematous sheath is often diagnosed erroneously as due to a balanoposthitis when no inflammatory lesions are present. Balanoposthitis due to bacterial agents are uncommon in stallions even though various infectious agents may be carried from mare to mare on the penis and prepuce. Early symptoms of dourine, a reportable venereal disease of horses transmitted by coitus, are swelling, edema and reddening of the penis and prepuce. This disease, not seen in the U.S., is caused by *Trypanosoma equiperdum*. Later in the disease process depigmentation of the skin of the genital organs may occur.⁸

An equine venereal balanitis and vulvitis, formerly called genital horse pox or coital exanthema, caused by a herpesvirus has been described.^{9,13} (See Figure 147.) After an incubation period of 6 to 8 days circular, confluent, poxlike lesions occur on the skin of the penis. These lesions heal in 10 to 14 days if secondary infections do not occur. Depigmentation of affected areas is common. There is no effect on fertility but affected stallions may refuse or hesitate to copulate. Withholding affected stallions from service to prevent the spread of infection to susceptible mares and local conservative treatment of the lesions is indicated. One attack does not confer a permanent immunity.¹⁸ This virus is not the rhinopneumonitis virus. The disease is occasionally seen in the U.S. especially on breeding farms where it may spread rapidly by coitus or grooming.

Cutaneous habronemiasis, summer sores or genital bursatti may affect the equine penis and prepuce. The Habronema larvae may produce fungoid granulomatous growths 1 to 3 cm. in diameter that may contain firm

necrotic, irregular-shaped masses or "kunkurs." These lesions bleed readily on manipulation.^{18,31} The lesions are not seen on the genitals of mares. These lesions may produce intense pruritus. In some cases their presence near the urethral process results in difficult frequent urination with spraying similar to that produced when the urethral diverticulum is distended with smegma causing compression of the urethra. In the colder northern states these lesions subside and usually disappear during the winter months. These granulomas may be treated by topical organophosphates, amputation of the penis or the urethral process depending on its size and location.^{14,31} Local treatment with camphophenique in scarlet oil or an organophosphate preparation daily and a systemic organic phosphate insecticide ("Ronnel") at a dose of 90 mg/kg by stomach tube repeated in two weeks was recommended.³⁶ In countries where the screwworm or *Cochliomyia* fly is present, severe infestations of the sheath and glans penis of geldings or stallions may occur resulting in pain, bleeding and swelling. Good restraint, often requiring general anesthesia, is necessary to get adequate exposure for local treatment of lesions with Smear 62 or camphophenique. Further infestation should be prevented by confining the animal in a barn and treating the external preputial opening with fly repellent. Multiple, small ulcerous lesions on the penis and prepuce of a horse associated with spirochetes was reported.²³ The lesions healed in about three weeks and the spirochetes disappeared. In some horses excessive accumulations of smegma within the prepuce may be associated with a keratin-like coating of the penis and prepuce. Manual cleansing of the equine sheath with soap or oily antiseptic solutions is accomplished by restraint and the liberal use of cotton swabs. Wearing plastic or rubber gloves is advisable because of the odor of the smegma. Occasionally a heavy growth of *Pseudomonas* and/or *Proteus* organisms are present in the equine sheath causing an objectionable odor and excessive smegma. Regular cleaning of the sheath with mild soap and water and occasional application of neomycin, or a similar antibiotic, in a vegetable oil vehicle may be indicated.

Balanoposthitis seldom occurs in the boar. The preputial diverticulum in the boar often fills with foul-smelling urine and smegma and externally may resemble an umbilical hernia. (See Figure 160.) This can readily be differentiated from a hernia on clinical examination by squeezing the enlarged diverticulum and expressing its odoriferous contents. In boars concretions and preputial calculi and diversion of the penis into the preputial diverticulum occasionally were present, causing difficult urination and inability to protrude the penis.¹⁹ Extirpation of the preputial diverticulum of boars will markedly

reduce the bacteria in semen collected for artificial insemination and also greatly reduce the boar odor.^{1,19} The boar's sheath may become infested with screwworms. In pigs with hog cholera ulcers of the prepuce as a result of infarction have been reported.¹² Ulcerations of the porcine penis due to other causes may be observed. These conditions in boars are usually easily diagnosed and treated. Surgical procedures for prolapse of the penis and extirpation of the porcine preputial diverticulum have been described.^{6,19}

In the dog, balanoposthitis is occasionally observed but seldom if ever, is a cause of failure of copulation. It is characterized by a discharge of pus from the prepuce and it usually responds well to mild antiseptic douches followed by bland antibiotic ointments or solutions. Balanoposthitis in the dog should be differentiated from the prostatitis as both are characterized by pus appearing at the preputial opening. Suppurative, ulcerative and follicular balanoposthitis or preputial catarrh is common in the dog.⁵ It is interesting to note that follicular lesions occur in the prepuce of the dog and are similar in nature to the enlarged lymph follicles or to the granular venereal disease lesions seen in the prepuce of the bull. (See Figure 173.) As noted under IBR-IPV infection of the prepuce and penis in bulls isolation of a herpesvirus from the sheath of dogs has been reported.¹⁰ Balanoposthitis in the dog, as in other animals, is due to mixed infections, trauma, foreign bodies, other general diseases, and debility. The malicious or ill-considered placement of a rubber band around a dog's penis causes great discomfort, severe balanoposthitis and even necrosis of the penis. In the dog acquired phimosis is less frequent than is congenital phimosis.⁵

The prognosis in balanoposthitis depends upon the severity of the trauma or the infection. In mild cases the prognosis is good. In severe chronic cases with adhesions between the penis and prepuce or between the prepuce and adjacent tissues, the prognosis is guarded to poor. Some males may be slow to regain their libido following a painful balanoposthitis.

Treatment of mild cases of balanoposthitis may consist of douching the prepuce with aqueous or oily antiseptics or antibiotic preparations such as saline, 50 to 200 ppm. of chlorine solution, 1:2,000 acriflavine or very dilute potassium permanganate solutions, 1 percent hydrogen peroxide solutions, one ounce of bismuth formic iodide in a 500 ml. of mineral oil, 1 gm. iodine in one gallon of mineral oil, infusions of aqueous furacin and other antibiotics in oil in about 25 to 100 ml. volumes. Caustic or irritating antiseptics should be avoided. Treatments may be repeated at daily to weekly intervals. In cases of severe balanoposthitis with extensive necrosis

of the prepuce and penis adhesions may result if frequent oily antiseptics or antibiotic ointments and systemic antibiotics are not employed. Regular gentle protrusion of the penis may be desirable to prevent possible adhesions. Tranquilizers, anesthetics, pudendal nerve block, electroejaculator, and adequate restraint are helpful in applying treatment for balanoposthitis. Sexual rest is essential during and for sometime after the treatment of acute balanoposthitis to promote recovery and to prevent a loss of libido associated with the painful condition.

Miscellaneous Causes for Loss of Libido or Inability to Copulate include: 1) hernias 2) premature erection 3) short penile bone (dog) 4) loss of sensory innervation of the glans penis 5) vascular shunts causing failure of erection 6) urinary calculi and 7) other causes.

1) Umbilical and ventral hernias as well as a deep pendulous abdomen may interfere or prevent normal copulation by affecting the entry of the penis into the vagina at a natural mating. Umbilical and small ventral hernias may respond to surgery but since umbilical hernias may be hereditary the affected male should not be used as a sire. About 1 percent of Santa Gertrudis bulls and Holsteins in Australia have umbilical hernias.¹⁴ These affected animals should be culled and not operated upon. Extensive unilateral hernias or a deep "paunchy" abdomen usually observed in older bulls or rams may interfere with normal intromission and thrusting especially if arthritic lesions are also present. Marked reduction of roughage and bulky feeds is indicated in these males but the prognosis is usually guarded to poor.

2) Premature erection may occur in the dog, stallion and certain bulls and interfere with normal intromission. Premature erection in the dog as an obstacle to coitus and a cause of impotency has been described.¹¹ Complete erection normally does not take place until the canine penis is in the vagina. Artificial insemination was recommended as the quickest and easiest solution for this problem.¹¹ In stallions the glans penis occasionally becomes too large by "flowering" or "belling" to readily enter the mare's vulva. This cause of inability to copulate can usually be overcome by helping to direct the penis into the vulva before it becomes fully erect or by lubricating the vulva. As described previously certain beef bulls with a strong sex drive and with a narrow penis develop a "corkscrewing" or coiling of the free end of the penis at premature full erection that prevents intromission. (See Figure 165)

3) Occasionally a dog will have a short penile bone with a long flaccid cranial portion of the penis that is difficult to direct into the vulva at coitus.⁹

4) Loss of sensory innervation of the glans penis prevents natural intromission and the "thrust" reflex nec-

essary for ejaculation and leads to a pronounced decline in sex drive. Lack of sensation of the glans penis may be caused by injury to the dorsal nerve of the penis secondary to rupture and hemorrhage of the corpus cavernosum penis, by the improper technique of injecting local anesthesia on the dorsal nerve of the sigmoid flexure of the penis, occasionally by an operation to correct the spiralling of the bovine penis or by a rubber band from an artificial vagina or other source that is placed around the penis and not removed for several days. Lack of sensation of the glans penis may also be due to necrosis of the mucosa of the glans secondary to severe balanitis of an infectious etiology or due to trauma resulting in severe scarring. Amputation of the glans penis by a rubber band or following extensive surgery for a tumor produces the same local "anesthetic" effect. Males that have had experience breeding before the loss of sensation in the glans penis remain sexually active but suffer from a definite loss of libido. Immature males with a similar loss seldom show much sexual desire as demonstrated by mounting and actively seeking the vulva with their penis. In bulls topical anesthesia of the glans penis caused intromission to be difficult and delayed but copulation occurred. Topical anesthesia of the glans as well as the free portion of the penis blocked the ability to copulate. Infiltration of the glans penis with a local anesthetic prevented ejaculation. Bulls with unilateral dorsal penile nerve neurectomy were able to copulate but time to ejaculation was prolonged. Bulls with bilateral neurectomy were unable to copulate.⁴ Thus it is possible the bulls may recover from a hematoma or penile surgery and in a few weeks or months develop signs of decreased ability or inability to copulate due to adhesions around the penile nerves with secondary degeneration due to subsequent injury or stretching. An experimental study of the results of desensitization of the glans penis in the cat was reported.¹ Damage to the nerve supply of the ischiocavernosus muscle may cause its atrophy and result in the inability of the penis to become erect.

5) **Vascular shunts causing failure of erection.** In bulls exhibiting a flaccid penis or only a partial erection that was lost rapidly during attempts at natural service or on stimulation with an electroejaculator before intromission or full erection was accomplished often were shown to have shunts between the corpus cavernosum penis and the extrocarporeal circulation of the penis.²⁵ Some of these shunts were acquired after rupture of the tunica albuginea of the penis and hematoma formation with spontaneous healing, deep lacerations of the penis and surgical operations to correct penile deviations. In other bulls multiple shunts of a congenital nature were observed in the distal portion (glans) of the penis. Serial

contrast radiography confirmed the suspected diagnosis,^{22,25} and surgical correction was described for valuable bulls with only one or a few shunts. Using a wedge resection of the tunica albuginea, surgery was successful in 4 of 8 bulls.²⁵ English workers described 6 bulls in 3 breeds with good libido but 5 were unable to erect the flaccid penis to protrude it from the sheath. This was caused by major venous drainage of the corpus cavernosum penis by the dorsal venous system.³ A similar impotence was reported in five boars with inability to obtain or sustain penile erection and copulate. This condition was developmental in origin with abnormalities of the dorsal venous system allowing blood to drain from the corpus cavernosum penis.²

6) Urinary calculi lodging in the urethra may occasionally be a cause of acute pain, obstruction and rupture of the urethra in male domestic animals and cause reluctance to copulate and inability to ejaculate. Urinary calculi were described in a bull with inability to copulate and exhibiting impotentia coeundi.²¹ The author has observed several bulls with urethral calculi, that refused to copulate and one that copulated and bled from the urethra. In cases of urinary or urethral calculi the prognosis for the future breeding life of the male is grave. Although an operation can be performed and the calculi removed, suturing of the urethra often results in a stricture. When the urethral and skin incisions in the bull are left open to heal by second intention, in order to save the animal for future breeding an urethral fistula or strictures often form. Other calculi may lodge in the same area; or adhesions form in the region of the sigmoid flexure and the ability to protrude the penis is lost. Leaving the skin and urethra open to heal by second intention is however occasionally successful in the dog and has been reported in the bull. Depending on the location of the urethral fistula the male may be unable to properly place the semen in the vagina. A urethral calculi retriever (Haver-Lockhart Lab., Shawnee, Ks.) modified after a human retriever for urethral calculi has been described.¹⁵ This has proven successful in cases where tranquilizers and muscle relaxants when administered early failed to result in the passage of the calculi from the usual site of lodgement at the sigmoid flexure. The bull is placed in lateral recumbency under tranquilization. Pudendal nerve block may also be used. The penis is fully extended and the retriever with proper lubrication is passed beyond the calculi and then withdrawn removing the obstruction. Stricture formation was reported not to be a serious problem.

In the ram calculi may lodge in the sigmoid flexure area as in bulls but are more commonly found in the urethral process. Amputation of the urethral process just

proximal to the calculi is usually performed. If most of the urethral process is removed conception rates might be markedly reduced due to poor distribution of semen in the vagina at the time of ejaculation.¹³

Calculi are common in the male cat¹⁶ and uncommon in the dog.⁶ In order to preserve the breeding potential of these animals conservative therapy such as massage and flushing in the removal of the urethral calculi and in the aftercare is indicated, surgery should be used only as a last resort. The use of a loop of no. 26 twisted steel wire to remove urethral calculi and mucous plugs in the anesthetized cat has been described.⁵ Up to 1 percent of male cats may develop calculi and recurrence is common.^{16,17} Using a 3" nasal lacrimal duct needle rather than a tom cat catheter and small amounts of 50 percent vinegar in water to remove urethral calculi from anesthetized cats was recommended.^{16,17} There was experimental evidence that several infectious viral agents were important etiologic factors along with other environmental and nutritional factors.^{16,18} Antibiotics such as chloromycetin, reduction of minerals in the diet, lowering the pH of the urine and increasing the water intake and other conservative therapeutic measures¹⁶ may be helpful in controlling urolithiasis in these animals. In the dog calculi tend to lodge at the caudal end of the os penis since the urethra passes along the ventral groove in the penile bone.^{10,23} Urinary calculi ruptured urethras and bladders, greatly enlarged bulbourethral glands and vesicular glands in footlot lambs or wethers given 12 to 15 mg. implants of stilbestrol or 2 to 5 mg. of stilbestrol daily in the feed was reported.^{12,20} This occurred as early as 10 to 14 days after the administration of the stilbestrol.

6) Pain caused by infection of the genital organs or peritoneum may be a cause of impotency or refusal to copulate. A stallion with infection of the ampullae and seminal vesicles refused to copulate.²⁴ The author has observed several bulls with severe acute semino-vesiculitis that were slow or refused to mount. Two boars with brucellar orchitis refused to copulate and two more had a markedly reduced libido.⁸ Acute prostatitis in dogs might similarly affect copulation. Necrobacillosis of the liver and traumatic gastritis with acute peritonitis may be associated with failure or refusal to copulate in bulls. Severe congenital or acquired cardiac diseases often result in dyspnea and inability to perform coitus by male animals.

Reduced to Complete Lack of Sexual Desire and Inability to Copulate

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Incapacity or Reduced Capacity to Fertilize in Males, Including Hereditary Disorders: (Impotentia Generandi)

Fertility is the normal functioning of the testes, accessory glands and ducts to deliver sperm of normal quantity and quality. Fertility and potency are not correlated or related and may be divergent in the same male animal. Infertility or sterility in males is usually characterized by normal sexual desire and the ability to copulate and ejaculate, but a complete or abnormally high percentage of failure of fertilization or conception, or delayed returns to estrum indicating early embryonic death in the females.

Although most of the causes of incapacity or reduced capacity to fertilize in males is due to acquired diseases or pathological lesions, a significant number of causes are congenital or hereditary and should be recognized to avoid their perpetuation or increase in future generations. Some of these hereditary conditions causing a mild or moderate problem in young males, such as hypoplasia of the testes, can predispose the male to testicular degeneration and more severe infertility or sterility. Excellent reviews of the inherited disorders of cattle related to infertility and fertility have been published.^{12,25}

The incapacity or reduced capacity to fertilize may be characterized by either of two findings following a complete semen examination. In one the semen is essentially normal on examination, and in the other the semen is abnormal in morphology, concentration, motility or other qualities. The former condition is often difficult to explain satisfactorily with our present knowledge; however, recent findings in cytogenetics and electronmicroscopy have indicated several promising leads.

Impotentia Generandi Associated with Apparently Normal Semen Production in cattle has been reviewed

in Chapter XIII in the discussion of herd infertility, "repeat breeders," or failure of conception in females following service by bulls infected with brucellosis, vibriosis, trichomoniasis, and possibly IBR-IPV virus, mycoplasma, ureaplasma or other organisms. Active brucellosis in a herd of cattle is associated with symptoms of infertility; and the intrauterine insemination of brucella-infected semen usually results in infertility. Boars infected with *Br. suis* may carry and transmit the organisms to the female at coitus resulting in early embryonic death and signs of infertility as well as abortions. After examining 828 bulls for infertility in 1953 it was determined that 374, or 45.2 percent were affected with vibriosis or trichomoniasis.²² In this series of cases, however, only 15 of the 374 bulls had trichomoniasis. Sixty percent of 105 herds in all parts of Sweden in 1955 were or had been infected with vibriosis.⁷ The incidence of vibriosis in naturally-bred herds, especially beef herds, in the United States is possibly equally high.

A number of herds with infertility resembling vibriosis were investigated but without finding the cause.¹⁰ Another study reported on herd infertility problems arising in 47 herds in which no diagnosis could be made because no pathological conditions were found in the bulls or cows to explain the sterility.²² Errors or deficiencies in management, as discussed in Chapter XIII may also be the cause of widespread infertility in some herds. Infertile, disease-free male animals with an apparently normal semen picture in regards to motility, concentration and morphology are uncommon if their reproductive management is good.

Abnormal acrosomes, knobbed spermatozoa, related to defective spermiogenesis involving the Golgi apparatus has been described in bulls, boars and dogs as a cause of infertility in semen with normal motility and concentration of spermatozoa. Certain of the stains or techniques used for preparing spermatozoa for morphological examination do not reveal this defect; while others such as nigrosin eosin, India ink or Giemsa show a refractile unstained or lightly stained area in the anterior pole or acrosome of the head of the spermatozoa. An eosin B. and fast green stain of the acrosome of spermatozoa permits examination by a light microscope.^{23,24} Certain sterile Swedish Landrace boars had as many as 80 to 90 percent of their spermatozoa with an acrosomal, knobbed defect.³ Males with about 50 percent of their spermatozoa with acrosomal defects had low fertility. Phase contrast microscopy revealed these defective acrosomes. Sometimes the anterior border of the spermatozoa was flattened due to a protrusion and bending over of the acrosome.³ Nearly all of the spermatozoa in some bulls were affected. The defective acrosome apparently

rendered the sperm cell incapable of penetrating and fertilizing the ovum.⁸ The nature of this defect in bulls was seen under the electronmicroscope has been illustrated.^{3,6,8,19,20} This defect in spermiogenesis is apparently due to an autosomal recessive sex-linked defect in Friesian cattle.⁹ This defect has been reported in a sterile Boxer dog and in Charolais and Holstein bulls in the U.S.¹⁸ (See Figure 178.) This defect was described in two subfertile bulls, a Holstein and a Jersey.²⁰ They had nonreturn rates from AI of 40 and 59 percent, respectively. Three of four sons of the Holstein bull were similarly affected. In the latter Holstein bull 0.3 to 6.2 percent of the spermatozoa had knobbed acrosomes, 1.7 to 9.1 percent had ruffled acrosomes and 2.1 to 21.9 percent had an incomplete or missing portion of the acrosome. This was a defect in spermiogenesis and could be seen in the spermatids.^{19,20} Aging of spermatozoa also produce acrosomal changes and infertility.²¹

Two nearly sterile bulls had semen with normal motility and concentration of spermatozoa. After staining with opal blue and examining the stained cells with a phase-contrast microscope, eversion of the galea capitis and crater-shaped depressions in the nucleus were found.¹ Apparently similar invaginations of the nuclear envelope in the bull and the boar were described that were associated with a severe disturbance of spermiogenesis with many other abnormalities of the sperm cell.⁵ Feulgen stain and phase-contrast microscopy revealed these invaginations to be located near the anterior border of the post-nuclear cap in the equatorial segment of the sperm head. These crater-shaped depressions in the nucleus have been the subject of further studies in which depending on the type of staining and microscopy have been called "diadem sperm," "pouch formations," nuclear lesions and vacuolar defects.^{8b,18b} The percentage of affected spermatozoa in ejaculates is variable. When over 20 to 30 percent of sperm cells are affected, fertility is moderately to severely reduced even though the motility and numbers of spermatozoa were normal. This defect apparently is not hereditary, but the cause is not known. Special staining and examination procedures are necessary to observe these nuclear lesions.

A sterile Ayrshire bull produced sperm cells with normal motility and concentration but with up to 20 percent abaxial tails and 17 percent swollen midpieces.² Even though the concentration and motility of sperm cells in the ejaculate is normal, special staining and examination of cells from infertile males is indicated.

Studies in cytogenetics have shown that gene or chromosome defects may occur at the time of meiosis and result in infertility. An apparently normal semen picture may accompany these defects. Certain bulls with excel-

lent appearing semen in which genital infections were excluded had a low fertility due to intrachromosomal aberrations.^{15,16} The spermiogenic epithelium showed a cytologic picture indicative of structural changes in the chromosomes including translocations and inversions. Although affected spermatozoa may fertilize the ovum, the zygote will often lack a balanced gene complement and death often results at an early stage of gestation or this defective chromosome complement may be carried into the next generation where usually about 50 percent of the male individuals are affected with infertility. Some offspring from affected bulls may be completely normal. Generally the greater the number of genes involved in translocation or inversion the greater the degree of infertility. In affected bulls diagnosis at present can only be made with an electronmicroscopic study of the germinal epithelium. By this technique acquired disturbances in spermatogenesis can be distinguished from the congenital or constitutional disturbances. These forms of sterility represented only a small number of all those that actually occurred.¹⁶ Gustavsson¹³ reported on a translocation defect of the chromosomes in the Swedish Red and White breed of cattle. About 14 percent of the cattle were heterozygotes and 0.34 percent were homozygotes for the translocation. Daughters of translocation sires exhibited a greater infertility rate, apparently due to early embryonic deaths, than daughters of normal sires.

The metaphase and anaphase figures from the meiotic divisions of the spermatocytes in the seminiferous epithelium in 4 boars and 7 bulls with normal semen pictures that were relatively or completely sterile were analyzed.¹⁴ Two boars had acrosomal defects of their spermatozoa. This study concluded that even though some chromosome changes were apparent, the primary or principal cause of defective spermatozoa was to be found in the nonchromosomal structures, namely the divisional apparatus.

The relationship of spermatozoal DNA and male infertility has been reviewed.¹¹ The conclusions are presently equivocal. A group of stallions with impaired fertility with semen of normal quality were studied.¹⁷ The infertility might have been caused by an inherent enzymatic disturbance that resulted in the early death of the sperm cell in the female genital tract.

These above preliminary studies on infertile males with essentially normal semen and spermatozoa have indicated that defects in genes and chromosomes especially during meiosis, and developmental defects of the sperm cell during spermiogenesis may occur. Future studies in the fields of cytogenetics, cellular biology and electronmicroscopy will undoubtedly further elucidate the mechanisms of male infertility occasionally associated with an

apparently normal or nearly normal semen picture.

Impotentia generandi associated with abnormal semen production is much more commonly observed and is due to pathology of the testes, the epididymis, the ductus deferens, the accessory glands and the urethra whereby sufficient numbers of healthy fertile sperm cells are not deposited properly at the time of coitus to cause the fertilization of the ovum and the normal development of the embryo. Abnormal semen may be due to congenital, hereditary or acquired causes. The latter are the most common. The former is highly important in the selection of sires because of the genetic implications. Occasionally both groups of causes are involved in an infertile male.

Pathology of the Testes with Abnormal Semen Production, Hypoplasia

Prior to the work of Lagerlof in 1934¹² studies on the pathology of the testis were incomplete and generally limited to the more obvious and severe clinical lesions such as orchitis and fibrosis. Since then a great amount of work has been done on correlating semen abnormalities with testicular pathology. The two are closely related and semen examinations reflect fairly accurately the conditions present in the seminiferous tubules of the testes. However, it is necessary to consider that it requires about 60 days from the first stages of spermatogenesis to the ejaculation of spermatozoa.

Lagerlof¹² divided the pathological conditions affecting the testis proper into testicular hypoplasia, testicular degeneration, testicular fibrosis, and testicular inflammation. The author believes that since testicular fibrosis usually follows testicular degeneration and testicular inflammation, and since testicular inflammation usually produces an acute, severe testicular degeneration, testicular fibrosis and testicular inflammation should be considered under testicular degeneration. If this classification is accepted then the two most common changes occurring in the testes causing disturbed spermatogenesis are hypoplasia, which is congenital or hereditary, and degeneration of the seminiferous tubules, which is usually acquired but may be predisposed by genetic defects, weaknesses, or inherent constitution.

Testicular pathology due to congenital or hereditary causes includes hypoplasia, certain defects in the seminiferous tubules and sperm cells including cytogenetic and chromosomal defects, cryptorchidism and inguinal hernias. The latter two conditions interfere with the normal thermal regulation of the testes which results in sterility or infertility.

Hypoplasia of the testes is observed occasionally as a unilateral or bilateral condition at the time of puberty, or later, in all domestic animals. It is noted most commonly in bulls, rams, boars and stallions. Testicular hypoplasia was a cause of 23 percent of the testicular pathology in Swedish bulls; this did not include the cases of inherited testicular hypoplasia of the Swedish Highland breed.¹³ This is a slightly higher incidence than the 12 to 17 percent given by other workers.^{1,9,14b,20} The hereditary type of hypoplasia affected as many as 25 to 30 percent of the male and female animals of the Swedish Highland breed, a polled breed.¹³ Gonadal hypoplasia in this breed was largely limited to those cattle that were 90 percent or more, white.¹⁷ Cattle with black ears were not affected. In these white cattle hypoplasia of the left testis occurred in about 25 percent of all the bulls, in the right testis in 1 percent, and in both testes in 4 to 5 percent. This condition is due to a single recessive autosomal gene with incomplete penetrance.⁷ A similar widespread condition affecting the gonads of both males and females of a breed has not been described outside of Sweden.

Most workers agree that testicular hypoplasia is congenital and possibly hereditary in origin and is caused by a marked lack of, or reduction in, spermatogonia in the gonads during fetal life. Hypoplasia may be partial or total due to a failure of germinal cells to develop in the yolk sac, failure to migrate to the gonad, failure to multiply in the gonad or that undergo extensive degeneration after they have entered the gonad. Unilateral or bilateral hypoplasia in bulls of both beef and dairy breeds and in other species have been observed occasionally in the United States but the incidence is generally low and the condition is sporadic. (See Figure 176 and 177.) In a few instances a familial trend was noted. It has been reported that dwarfs or beef cattle with a dwarf tendency are likely to show evidence of testicular hypoplasia. Some valuable beef bulls with unilateral testicular hypoplasia have been used as breeders and may produce as many as 20 percent of offspring with hypoplasia and poor quality semen.³ Marked hypoplasia of the testes, 10 percent by weight of normal testes, may occur in bulls, boars, rams, dogs and tom cats with the rare XXY karyotypic syndrome or human Klinefelter's syndrome.⁶

The symptoms of testicular hypoplasia in bulls vary greatly. In most cases sexual desire is excellent and coitus is prompt. Because of this the owners may not suspect the sterility for some time. The degree of either unilateral or bilateral testicular hypoplasia varies from nearly complete hypoplasia and sterility to only slight and often unsuspected hypoplasia. Lowered conception rates are often evident in the latter bilaterally affected males.

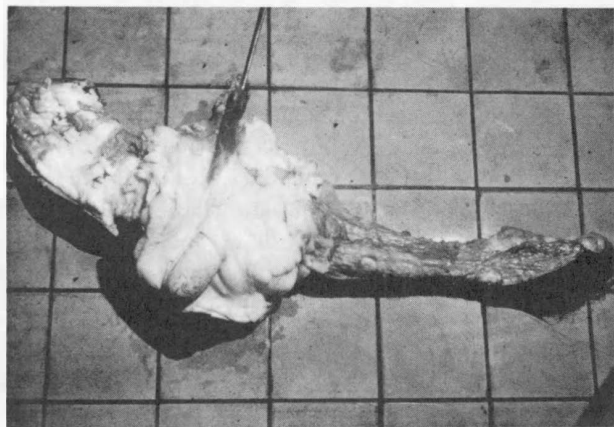


Figure 176. Bilateral Testicular Hypoplasia in a Fat 3-Year-Old Angus Bull.

Severe testicular hypoplasia is usually observed in young bulls one to two years of age. In sterile bulls with bilateral hypoplastic testes the semen is usually clear and watery with few or no spermatozoa. If the ejaculate is centrifuged and the sediment stained, giant cells and oftentimes medusa cells or ciliated cells from the efferent tubules may be observed. Giant cells or multinuclear cells with 6 to 8 nuclei apparently result from incomplete maturation divisions of the primary spermatocytes. The nuclei divide but the cytoplasmic divisions are not completed.⁵ These cells are seen in testicular hypoplasia and severe degeneration. The sexual organs develop nor-



Figure 177. Bilateral Testicular Hypoplasia in a 2-year-old Holstein Bull.

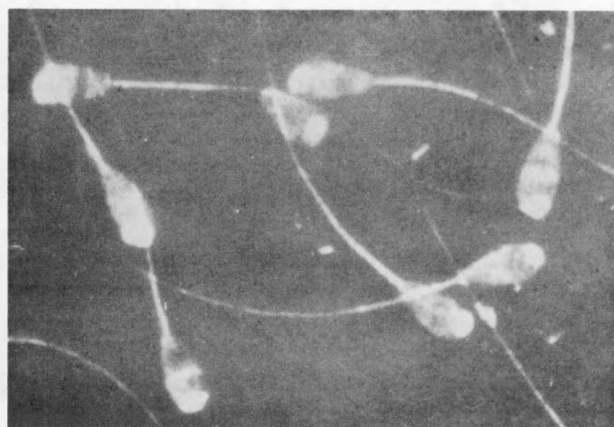


Figure 178. Abnormal Acrosomes or Knobbed Spermatozoa in a Sterile Bull. (Courtesy K. McEntee.)

mally except for the affected testes. Histologically the seminiferous tubules are very underdeveloped, with usually only the basal layer of cells being present.

Males which are severely affected with testicular hypoplasia are nearly sterile, but an occasional conception may occur in females bred to them. The semen picture shows a low concentration of spermatozoa, and the possible presence of a few giant cells. If azoospermia is present in repeated ejaculates complete sterility is assured. The affected testes are one-third to two-thirds normal size, but are usually firmer, or occasionally softer, than normal. (See Figure 177.) Histologic section reveals that one-half to two-thirds of the seminiferous tubules are undeveloped. Varying degrees of spermatogenesis may be present from spermatogonia, spermiocytes,

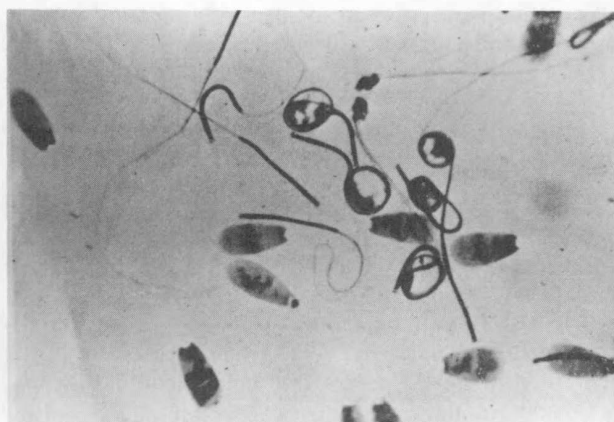


Figure 179. Lack of Intact Sperm Cells and Coiled Tails in a Sterile Guernsey Bull. (Spermatozoan motility was nearly absent.)

spermatids, to abnormal and normal mature spermatozoa. Three types of testicular hypoplasia in 3 inbred lines of Hereford cattle were studied.³ The first type was characterized by seminiferous tubules lined only with Sertoli cells. These bulls were sterile and the line became extinct. In the second line of bulls about 30 to 40 percent of the tubules were normal but only a few tubules were stage 8 with sperm cells lining the lumen. Reduced spermatogenesis was present. In the third line the bulls had reduced spermatogenesis, conglutination of spermatids and many giant cells. In another line of cattle the bulls had large firm testes but reduced sperm cell output due to blockage of the tubules before they entered the rete resulting in sperm stasis and atrophy of the seminiferous epithelium.

In some bulls with a moderate to slight amount of testicular hypoplasia the conception rate is low, about 20 to 40 percent. The testicles may appear nearly normal in size and consistency. The spermatozoan concentration is from 100,000 to 500,000 per cmm, the motility is usually low, and the number of pathological or abnormal spermatozoa is high, 30 percent or greater.

Depending upon the degree of hypoplasia, affected bulls will have a small firm epididymis especially in the tail region indicating reduced spermatogenesis and low gonadal sperm reserves. This will also be revealed by rapidly decreasing concentrations of spermatozoa in successive ejaculates.⁹ Slight or mild cases of hypoplasia with reduced spermatozoan concentration and motility predispose the bull to testicular degeneration. In some bulls sterility due to mild testicular hypoplasia may not be observed or become apparent until the bulls reach 3 to 4 years of age.

The spermatic cords of hypoplastic testicles are shorter as the testes are less heavy and the scrotum smaller than in normal males. Postpubertal bulls that have a scrotal circumference of less than 32 cm. should be suspected of having testicular hypoplasia or testicular degeneration with atrophy. In obese bulls with much fat in the inguinal region the thermal insulation so provided these hypoplastic testes might contribute to the infertility. (See Figure 176.)

Testicular hypoplasia may be erroneously diagnosed in young immature males that are underdeveloped or are retarded in growth at the generally accepted time of puberty for the species. The fertility and the percentage of normal spermatozoa produced increased from puberty to two years of age in beef bulls.¹⁵ The diagnosis of testicular hypoplasia should not be made before two years of age in the bull and horse or before one year of age in the boar, ram, dog or tom, unless the hypoplasia is marked and the male is well-grown.

Testicular hypoplasia and atrophy were observed in about 3.4 percent of 9,000 rams examined in Australia.⁸ The condition was usually unilateral and of a permanent nature. The spermatic cord was usually short and the affected testis was drawn up toward the inguinal canal. The consistency of the testis was either soft and flabby, or hard, indurated and fibrotic. The testes were decreased in size. The semen was always abnormal, with an increased number of abnormal spermatozoa and small, round, non-nucleated, germinal epithelial cells. An association between this type of testicular hypoplasia and unilateral cryptorchidism was suggested. The fibrotic small testes in some of the rams described above might have been due to trauma or other causes, producing secondary, degeneration and atrophy.

Sterility in boars is relatively uncommon.¹⁰ In 30 boars with testicular pathology, 8 or 26.6 percent had hypoplasia. These were young boars that were sterile or of very low fertility. A genetic or hereditary factor was probably present in hypoplasia in boars.¹⁰ Young boars may only ejaculate 2 to 3 billion spermatozoa when they are bred 2 to 3 times a week. If they are bred more often, the number of spermatozoa ejaculated may drop below 2 billion and infertility result. At 10 to 12 months of age most boars have matured sufficiently so that large numbers of spermatozoa are produced and infertility due to oligospermia is not a problem.^{1a,18} In cases in which semen examination was possible, spermatozoa were either absent or present in low concentrations of 20,000 to 70,000 per cmm. The number of pathologic spermatozoa was not high but there was a large percentage of immature sperm cells with a protoplasmic droplet on the middle piece. The motility was usually poor. The average weight of the hypoplastic testes was 226 to 240 gm., while normal testes weighed 594 to 632 gm. Histologic examination showed hypoplasia varying from only a single layer of germinal cells to widespread changes in the seminal epithelium.

Eunuchoidism or complete lack of sexual desire, may rarely occur in dogs, men and bulls with testes in the normal position or in unilateral or bilateral cryptorchidism.^{2,17a,21} The testes are small and atrophic. The interstitial cells are hypoplastic or fail to secrete androgen. In man eunuchoidism is characterized by low plasma concentrations of FSH and LH.^{17a} Testosterone given parenterally will produce secondary sex characteristics but the male relapses to the eunuchoid state if injections are discontinued. This condition may have been due to the **XXY or Klinefelter's syndrome** in animals or to **testicular feminization** due to a defect in the androgen receptors and characterized by a feminine appearance, retained testes, a normal vulva and vestibule, rudimentary

accessory reproductive organs and an XY karyotype.^{16b,17a}

Hypoplasia associated with a decrease in interstitial cell activity and a failure of normal antler growth in white-tailed deer in southwestern U.S. was reported.¹⁹ Testicular hypoplasia in the dog and cat is seldom described. Gonadal hypoplasia in a strain of grey collies that also had abnormalities of the blood, eyes and digestive tract was described.⁴

In the diagnosis of testicular hypoplasia, especially where it may be associated with a lack of sexual drive, the stage of development of the male and whether or not puberty has occurred must be considered. Testicular hypoplasia may be diagnosed erroneously in young, poorly-fed, slow-maturing males, especially of *Bos indicus* breeding.

The prognosis in testicular hypoplasia is poor. Affected animals should not be used for breeding because the condition may be hereditary. Severely affected animals are sterile or highly infertile. Mildly or moderately affected animals may have only a lowered fertility but are more prone to early testicular degeneration. Libido is usually normal or excellent. The numbers of motile normal spermatozoa per ejaculate or insemination largely determine the fertility of the animal in question not the percentages of the dead, poorly viable, immotile and abnormal spermatozoa.

The treatment of testicular hypoplasia in animals has been unsuccessful. The germinal epithelium of these affected animals apparently cannot respond to gonadotropic therapy because spermatogonia are lacking or reduced in numbers.

Hereditary or Congenital Sperm Cell Defects, Male Intersexes and Cryptorchidism

Sperm cell defects, possibly heritable, have been described in male domestic animals in which a large percentage of spermatozoa produced by a male are similarly affected.

Returned tails and narrow heads were reported to be hereditary in certain bovine families of the Jersey breed exhibiting much sterility.² Another study¹² also reported on infertile Jersey bulls with coiled or returned tails with a lowered motility rate. With repeated frequent ejaculations the numbers of abnormal sperm cells was greatly reduced. The defect in these bulls was apparently genetic. These defects may be similar to the Dag-effect.

Dag defect—Danish workers have described 15 related bulls, tracing back to a common ancestor born in 1934, in the Danish Jersey breed that had a low initial

spermatozoan motility of 10 to 15 percent and very poor fertility. These bulls had about 40 to 50 percent of their spermatozoa with strongly coiled, folded or split tails, the Dag defect.⁹ The fibers in the axial filament were normal in the testis but abnormal when the cells reached the cauda epididymis. This defect was shown to be due to an autosomal recessive factor. The defect developed in the distal part of the head of the epididymis.⁹ An infertile Holstein bull with a normal volume and concentration of semen but only 10 to 20 percent motility was studied.^{11b} About 25 percent of the spermatozoa had tail abnormalities somewhat resembling the Dag defect with an aberrant, defective arrangement of the fibrils. There was no evident abnormality of the seminiferous epithelium. A Canadian worker reported on three unrelated Hereford bulls with this Dag defect.¹³

The "tail stump" defect of spermatozoa originally described in Holstein Friesian bulls in Canada,⁶ and then in bulls in Denmark⁵ and India and recently in rabbits, a stallion and a dog,^{1c} is caused by deranged spermiogenesis that results in a severe infertility or sterility. The head of the affected spermatozoa is normal but the middle piece and tail are markedly defective with a stub or stump appearance at the base of the head. This defect is caused by an abnormality on the centriolar apparatus that blocks normal formation of the midpiece and tail.^{5b} Spermatozoan numbers in the ejaculate are normal but motility is very poor depending on the percentage of "tail stump" spermatozoa which may vary from 20 to over 90 percent. Other sperm cell abnormalities may also be present such as loose or separate heads. There may be a cytoplasmic droplet around the "stump." This condition is possibly due to a recessive gene.^{1c,5b}

Corkscrew sperm defect—A nongenetic defect seen in the Red Danish, Jersey, Friesian and Aberdeen Angus breeds due to an irregular distribution of the mitochondrial sheath together with a high incidence of persistent proximal droplets in affected sperm cells was described.³

Pseudo-droplet defect—A "pseudo-droplet defect" seen in 5 related Friesian bulls was reported.⁴ From 7 to 26 percent of spermatozoa in affected bulls had rounded or elongated, thickened areas on the midpiece. Reduced motility and infertility increased as the bulls became older.

Lack of intact sperm cells was described in Guernsey bulls with a history of complete sterility.^{7,8} The ejaculates of these bulls contained practically no intact spermatozoa, but only free heads and tails. Motility was low. Intact spermatozoa were fewer than 5 percent of the total. All heads showed a deep indentation marking the point of separation from the tails. The middle piece was thickened and varying degrees of coiling of the middle piece and tail occurred. This disintegration or separation

of the heads and tails of spermatozoa in the sterile Guernsey bulls was associated with the migration of the protoplasmic droplet from the proximal to the distal end of the middle piece which occurred in the head of the epididymis.⁷ While there was no conclusive evidence that the defect was inherited, the evidence was very suggestive. Eight Hereford bulls with low fertility had a high percentage of tailless heads in their ejaculate.¹⁴

Acrosomal defects or knobbed spermatozoa have been described in bulls, boars and dogs. This defect has been reported as due to an autosomal recessive gene in Holstein Friesian bulls.^{11a} As described previously in this Chapter, certain stains and techniques are very helpful in diagnosing this defect in what often appears to be a normal semen sample associated with complete sterility or infertility.

Deficiency in tail development and lack of motility was reported in stallions of one Thoroughbred blood line in which the condition might have been genetic in nature.¹⁰ The author has studied two stallions with congenitally lowered fertility with 50 to 75 percent of their spermatozoa having a single abnormality; in one stallion, a Standardbred, a grossly defective midpiece and the other, a Thoroughbred, an abaxial attachment of the midpiece to the head in over 60 percent of the spermatozoa. In stallions abaxial attachment of the midpiece to the head of the spermatozoa is commonly observed and this usually is not associated with infertility in the stallion and boar as it often is in the other species of animals. (See Semen Evaluation.) A sterile Ayrshire bull with up to 20 percent abaxial tails and 17 percent swollen midpieces was described.^{1b} Sperm cell concentration and motility was normal.

Ciliary diseases in man and animals have been reviewed.^{1a} Many of these are congenital or hereditary diseases affecting all body cilia in the respiratory and genital tracts resulting in chronic upper respiratory infections and infertility or sterility. These ciliary diseases usually result in the immotile-cilia syndromes.^{1a} One of these in humans is called **Kartagener's syndrome** that is usually characterized by sterility associated with immotile sperm cells and other cilia in the body and in many cases **situs inversus**.^{1a,8a} The normal concentration of live spermatozoa is present. Two similar cases have been described in dogs.^{1a} This defect of the tail and midpiece resembles several other defects in animals characterized by living sperm cells grossly lacking in motility.

Inbreeding, Chromosomal Aberrations and Intersexes

Inbreeding generally results in reduced fertility accompanied by an increase in the number of abnormal

seminiferous tubules, lowered semen quality and hypoplasia.^{4,5,19} Inbreeding in dogs resulted in lower conception rates, lower numbers of pups whelped alive and in reduced ejaculate quality of studs by lower sperm counts compared to outbred dogs.²⁴ There were wide differences in fertility between inbred lines of cattle from a few with excellent fertility to those in which the line died out because of infertility. The response to inbreeding with respect to fertility is variable with each line or family. Inbred lines usually undergo a period of infertility or sterility and if the line does not become lost due to deleterious genes, the fertility of the remaining animals in the line is often fairly satisfactory.^{17a} Five inbred, related bulls showed a low sperm cell concentration and a large number of pathological spermatozoa with a reduced motility.¹³ The infertility in these bulls was considered to be due to an autosomal recessive gene. In identical twin bulls great similarity of the semen and spermatozoa, duration of motility, and frequency of abnormal sperm heads has been noted.^{1a} The great difference between identical twin pairs of bulls and the similarity of each bull of a twin pair indicated that the differences between the twin pairs as well as the similarities within the pairs, were genetic, since all were reared under similar conditions. Hereford, Angus, Holstein and Shorthorn bulls had the best conception rate in England.²⁵ In the United States and Canada Guernsey bulls generally have a lower conception rate than other breeds.² Nine of 19 Guernsey bulls used for artificial insemination had lower than average non-return rates, below 64% at 60–90 days. Two of these 19 bulls had 1/29 centric fusion with 59 chromosomes and 3 others had achromatic gaps and chromatid breaks.² In 743 young bulls examined cytologically in the U.S. no translocations were found.¹⁰ Other cytogenetic studies on bulls, horses and swine were reported.²⁰ Aneuploid cell lines in two related boars were associated with reduced litter size in their offspring as well as some of their daughters.²³

Cytogenetic disturbances in spermatogenesis caused two abnormalities in the primary spermatocytes including (1) "stickiness" of chromosomes in which they failed to separate at anaphase, and (2) a pyknotic nucleus and multiple spindle formation due to a dysfunction of the mechanism of cell division due to extra centrosome divisions resulting in the formation of giant cells with a number of nuclei.¹⁶ In both conditions the semen was thin and watery. In the former the semen centrifugate was made up almost entirely of pyknotic nuclei and was characteristic for this condition seen most often in the Swedish Lowland Holstein Friesian breed in which intensive inbreeding had occurred. The latter condition occurred in only a few bulls. The semen centrifugate was

composed of giant cells and pyknotic nuclei and these affected bulls belonged to the same family so a recessive gene might have been involved. As mentioned previously, the Gustavsson anomaly or a Robertsonian 1/29 chromosomal translocation occurred in Swedish cattle that resulted in a degree of infertility characterized by early embryonic deaths.¹⁴ A translocation anomaly in a boar was associated with reduced litter size.²⁰ Probably other primary cytogenetic disturbances of spermatogenesis occur and will be described in the future.

The male tortoise-shell, black and orange stripes or including white, tricolored or calico **tom cats** are uncommon because the genes for yellow or orange color are carried on the female, X, chromosome. However, rare male tortoise-shell cats have an abnormal sex chromosome constitution of XXY resembling Klinefelter's syndrome in man. This condition in cats has been well-described.^{11,18,22} These male cats have very small testes and are sterile due to failure of the seminiferous tubules to develop. One affected cat had no spermatogonia in the seminiferous epithelium. The possible incidence of male to female tricolored cats was 1:200 to 1:3000.^{11,18} Other types of chromosome combinations in tricolored male cats: XXY, XX/XY, XX/XX/XXY, XX/XXY, XY/XXY, and XX/XXY have been reported.^{11,18,22}

A recent study and review of male tortoiseshell and tricolored cats^{17b} indicated that those with the 39XXY karyotype were all sterile with very small testes, no germinal epithelium, no libido and no secondary sex characteristics. Those with a 38XY/38XX and 38XY/39XXY karyotypes had a variable fertility with libido and secondary sex characteristics. While those with 38XX/38XY karyotypes were fertile normal males. It was suggested that because of their coat color these cats were examined cytogenetically but other cats with a different color might also show chromosomal abnormalities.

A polled Hereford bull with good libido had very small, one-tenth normal-sized testes, azoospermia and a 61,XXY karyotype.⁷ This XXY or Klinefelter's syndrome seen in about 1 in 500 live-born human males has also been reported in rams, boars and dogs.⁷ Undoubtedly cytogenetic defects occur in stallions as have been described in mares but defects of the reproductive organs are much more obvious in stallions and seldom would these animals be selected for service.

Infertility in hybrids usually occurs when there are major differences in the chromosomes of the parents. Minor gene differences may be overcome so fertility is possible. The failure of gametogenesis in some hybrids is apparently due to asynapsis during the first meiotic division of the primary spermatocyte. Sterility is more common in the male hybrids. Even in some intraspecies

crosses where the chromosomes are nearly similar, hybrid fertility, particularly of males, may not result.^{1c} A common example of the above hybrid infertility in domestic animals is the horse and ass cross producing the hybrid mule, with chromosome numbers of 64, 62 and 63, respectively. Hybridization attempts in goats and sheep obtained conception but all the embryos died.¹⁵

In the bison x domestic cattle cross, as well as the yak X domestic cattle, and yak X zebu crosses, the bulls are likely to be sterile.^{6,12} This was believed due to the inheritance of the small, thick scrotum from the bison or yak causing an elevated scrotal temperature that adversely affected the large testes inherited by these hybrids from the domestic cattle or zebu that required a lower testicular temperature for the normal functioning of the seminiferous tubules. Recent cytogenetic studies indicate that chromosomal incompatibilities are more likely a cause for the infertility of these hybrid males.

In bovine twins of unlike sex the female twin or freemartin is sterile due to the vascular anastomosis with the male twin which is usually considered to be normal. (See Chapter IV.) Most bulls born cotwin with freemartins are chimeric with from 5 to 95 percent of their blood lymphocytes being XX cells. Of 12 chimeric bulls studied in an AI stud, 58 percent were culled for poor semen quality and infertility associated with testicular degeneration and hypoplasia.^{3,8} One of the infertile bulls had a skewed sex ratio of 29 males to 71 females suggestive of germ cell chimerism.⁸ Further study on bulls cotwin to freemartins is indicated.

Male intersexes are invariably sterile. Intersexuality may arise from aberrations of genetic or chromosomal origin, aberrations of gonadogenesis, and reversal of sex involving the accessory or external genital structures.^{1b} **Male pseudohermaphroditism** is found in the caprine, porcine and occasionally the bovine, equine and other species. **True hermaphroditism** is uncommon. In both horses and cattle this latter condition was characterized by ovotestes, no scrotum, an underdeveloped penis, uterine tissue and vesicular glands and chromosomal chimerism.⁹ True hermaphroditism is also seen in the other domestic animals including the goat, dog, pig and cat.^{9,22} In the Saanen and Toggenburg breeds of goats the incidence of intersexes varies from 5.8 to 14.9 percent. They have a wide range of abnormality from phenotypically nearly normal males to nearly normal females. This condition in goats is caused by a single recessive sex-linked gene linked to the dominant gene for polledness. (See Chapter III.) No case of a horned pseudohermaphrodite has been described. Most affected goats have testes, often intra-abdominal, and external genitalia of an intermediate type. They are genetic females (XX) with

positive sex chromatin. A high incidence of infertility in polled Saanen goats was described in which the recessive character caused pseudohermaphroditism in female goats and hypoplasia, sperm granulomas of the epididymis and a high percentage of sperm cell abnormalities in some male goats.²¹ The infertility problem in Saanen goats could be largely avoided by raising for breeding purposes only those goats with a horned parent.

Intersexes in pigs are common but not as common as in goats. They also are of the male pseudohermaphrodite type. The condition is probably caused by a recessive gene. The affected animals are genetic females, the testes are invariably intra-abdominal and externally a characteristic "fish hook" vulva with a prominent "clitoris" or phallus is present.^{19b} Male pseudohermaphrodites are also occasionally observed in cattle, horses, sheep and dogs.^{21a} Three affected sons of a Brown Swiss bull have been reported.¹²

Cryptorchidism in animals, if bilateral, results in sterility. In horses cryptorchids may be spoken of as "ridglings," "rigs" or "originals." Unilateral cryptorchidism is more common and usually results in near normal fertility because of normal sperm production from the testis located in the scrotum. The term "monorchidism" is incorrect and should not be used. Cryptorchidism or incomplete descent of the testis or retention of the testis occurs in all domestic species but is seen most commonly in stallions, boars, dogs, less commonly in rams and bucks, uncommonly in bulls, and rarely in tom cats. (See Chapter III.) The undescended testis may be located anywhere from just caudal to the kidney to within the inguinal canal. Many abdominal testes are located close to the internal inguinal ring. Often the loosely attached epididymis in the horse may have descended into the inguinal canal.

Occasionally testes not in the abdominal cavity, inguinal canal or scrotum may be located ectopically under the skin of the ventral caudal abdomen, especially in bulls, alongside the penis, or rarely in the femoral canal or in the perineal region. This is more commonly the case in male pseudohermaphrodites where no scrotum is present.

In some animals in which the testis is retained in the inguinal canal it will descend spontaneously into the scrotum in a few months to a year after birth. In a few cases in colts, testes may have descended into the scrotum at birth and later became cryptorchid and located in the inguinal canal. Although a noted veterinarian^{18b} has reported that the testes of newborn colts can invariably be palpated in or just above the scrotum, further study, confirmed by castration, should be undertaken since the gubernaculum is large in newborn foals. By 30 days after

birth the gubernaculum is greatly reduced in size and the testes can be readily palpated in most foals. It would seem very unlikely the descended testes at birth could, with time, assume the internal relationships found in abdominal cryptorchidism. All retained or cryptorchid testes are small, soft and flaccid weighing in the horse 25 to 131 gms.; normal descended testes usually weigh 170 to 325 gm.⁴ No spermatozoa are produced by the retained testis but well-developed or degenerate seminiferous tubules may be present. Spermatogenesis is completely inhibited by the elevation of the temperature of the affected testis. The interstitial or Leydig cells are not affected so sexual activity is normal or even exaggerated in some cryptorchids. Cryptorchid animals should not be used for breeding.

The Technical Development Committee²⁰ in England reported that cryptorchidism in the horse is inherited in a dominant manner while in the other species it is a recessive trait. Unilateral cryptorchidism more often affects the right testis especially in dogs, possibly because the right testis develops in the embryo a greater distance from the scrotum.⁵ In 4 studies,^{4,8b,11,19b} from university clinics it was reported that in over 1000 cryptorchid horses about 90 percent of the inguinal or abdominal testes were unilateral and of the abdominal testes about 70 to 75 percent were left-sided. These reports indicted that in about 60 percent of the presented cases the cryptorchid testis was intraabdominal. Based on his field experience the author strongly suspects this latter figure is biased. Many of these latter cases of cryptorchidism were probably referred to the clinics for specialized surgery. Most practicing veterinarians can detect inguinal testes by palpation assisted by heavy tranquilization and remove these retained testes by a slightly modified routine castration. Three of the cryptorchid testes contained teratomas or cysts, two of these were abdominal.⁴ Removal of cryptorchid equine testes has been well-described.^{1,2,11} The latter described a paramedian laparotomy approach for the removal of the abdominal testes.

In dogs cryptorchidism is seen most commonly in the brachycephalic breeds including: Boxers, Pomeranians, Dachshunds, Sealyhams, Cairn Terriers, and also in Whippets, Chows, Cocker Spaniels, Poodles, and others. The incidence of cryptorchid testes in dogs in England was reported to be between .05 to 0.1 percent.²⁰ In most dogs the testes are in the inguinal canal at birth and descend into the scrotum during the first week after birth. In some dogs the testes don't descend till near puberty.³ Possibly because dogs are maintained intact for many years, retained testes are predisposed to neoplasms. Sertoli cell tumors and seminomas in undescended testes tend to be more malignant.^{5,6,13,18} A highly

significant association of cryptorchidism and testicular tumors was reported with 58 or 53 percent of 108 Sertoli-cell tumors and 23 or 33.8 percent of 68 seminomas occurring in retained testes.¹⁸ These tumors affected the retained or abdominal right testes more frequently than the retained left testes. Dogs with scrotal testicular tumors were older than dogs developing cryptorchid testicular tumors.¹⁸ Signs of feminization were present in 16.7 percent, 50 percent, and 70 percent of the dogs with Sertoli cell tumors in the scrotum, inguinal canal and abdominal cavity, respectively. This may be due to the earlier detection and removal of affected testes in the external sites. Cryptorchidism and cryptorchidectomy in the dog and tom cat has been recently reviewed.²⁵ Tumors of undescended testes in man occurred 50 times more often than tumors of scrotal testes.⁸ Early removal of undescended testes is recommended.

Cryptorchidism in swine is a monogenic sex-limited recessive.¹⁵ To eliminate this condition in swine or other species, all parents of cryptorchid animals should be discarded as breeders. The incidence in swine may reach 1 to 2 percent in some herds. If affected pigs are fattened rapidly and sold at or before six months of age very little or no boar odor will develop in the carcass. In sheep cryptorchidism is seen in all breeds especially in inbred families, as it probably is due to an autosomal recessive or a dominant gene with incomplete penetrance. The incidence in sheep is 0.5 percent with 90 percent of unilateral abdominal cases involving the right testis.^{10a}

The rapid progress possible in the elimination of cryptorchidism, probably due to a recessive defect with incomplete penetrance, in flocks of Angora goats by rigid culling of parents and even close relatives of affected animals was described.^{19,23} An excellent bibliography on cryptorchidism in dogs and other animals has been compiled.¹² A few cases of left-sided cryptorchidism in Hereford cattle have been reported in which the condition appeared to be due to a dominant gene with variable expressivity.²⁴ Cryptorchidism is common in male fetal monsters and other defective individuals.

Treatment of cryptorchid animals, especially those where breeding is to be considered, should be discouraged. In humans where treatment is more frequently undertaken only those testes that would ultimately descend spontaneously would descend after gonadotropin therapy.⁸ Orchiopexy has proven to be a failure in producing satisfactory spermatogenesis.

Torsion or rotation of the descended testis is observed occasionally in the stallion^{17b} and rarely the dog.^{17c,d} It may be associated with an excessively long mesorchium, caudal ligament of the epididymis and the proper ligament of the testis. Torsion must be greater than 180°

to produce circulatory disturbances in the testis with strangulation and pain associated with a unilateral scrotal swelling and a stiff, "hiking" abduction of the rear leg in the affected side. It develops most frequently in the Standardbred but the author has observed the condition several Thoroughbreds. Apparently some horses at their racing gait are unable to draw the testis out of the scrotum. Suspensories have been tried on horses but are of limited value. Unilateral or bilateral castration is indicated.

Torsion or rotation of the retained or cryptorchid testes with strangulation of the spermatic cord is most commonly seen in the dog in association with testicular tumors, especially the Sertoli-cell tumor.^{17c} Symptoms may be acute or chronic with signs of abdominal pain and/or obstruction. Diagnosis is suspected by a retained or cryptorchid testis in an older dog and is confirmed by laparotomy. Torsion of a retained testis has been observed very rarely in the pig.

Manual torsion or "twisting" of ram lambs is an old castration technique of shepherds. The tail of the epididymis or ventral portion of the testis is manually rotated dorsally and then after several rotations of the testis around the tensed spermatic cord, the entire structure is pushed into the inguinal canal where it is retained and undergoes degeneration and atrophy due to the interruption of circulation.

Imperfect descent of the testes in cattle not associated with cryptorchidism has resulted in testes located horizontally and fairly high in the scrotum. This may be due to the attachment of the cremaster muscle to the caudal aspect of the testis, fixation of the distal end of the scrotum to the perineal region,²⁶ or lower than normal attachment of the gubernaculum. (See Figure 180.) This imperfect descent of the testes may result in impaired fertility with degeneration and atrophy due to difficulty of the thermoregulatory mechanism of the testes to operate properly. This condition might be genetic.⁷ Stallions that carry the testes high in the external inguinal ring may have low fertility for the same reason.

Multiple heterotopic nodules of testicular tissue scattered over the peritoneum have been described in a few pigs.²¹ These may be confused with a malignant neoplasm.

Scrotal or inguinal hernias, if large, may seriously depress fertility by markedly interfering with the normal thermoregulatory function of the scrotum and testes resulting in testicular degeneration. (See Testicular Degeneration.) If the inguinal ring and hernia is small there is a greater chance for strangulation of the intestine. Inguinal hernia is considered a common hereditary defect in horses and pigs; it is less common in bulls, dogs and

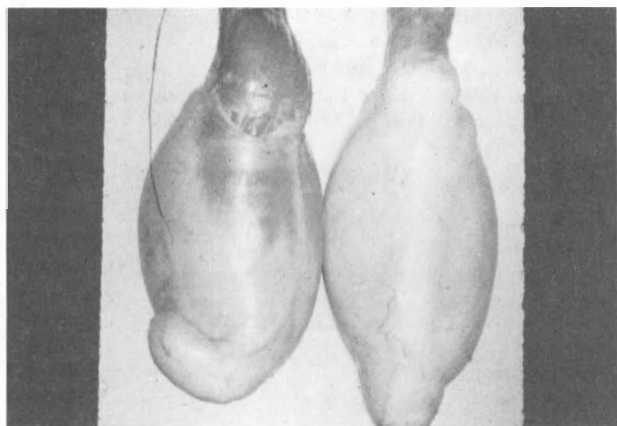


Figure 180. Abnormal Attachment of the Cremaster Muscle to the Left Testis Causing a Nearly Horizontal Position of the Testis High in the Scrotum (The right testis of the bull was normal).

rams, and rare in the tom cat. The incidence in swine was greatly increased from 7.5 to 43.2 percent in two generations by selective inbreeding.²² It was most common in the left side of the scrotum. Hernias usually appeared from birth to 30 days of age. It was considered to be a double recessive character. In cattle leftsided scrotal hernias were most common especially in the Hereford or Polled Hereford breeds.^{10,16,17} (See Figure 181.) In an inbred strain of Basenji about 75 percent of the pups had inguinal hernias.⁹ Animals with inguinal hernias should be castrated and not used for breeding. Reduction of the hernia and closure of the hernial ring can be performed through the inguinal canal, through an incision in the abdominal wall just cranial and medial to the ring or by a flank incision above the ring.



Figure 181. Left Inguinal Hernia in a Hereford Bull.

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Acquired Testicular Pathology

Testicular Pathology Due to Acquired Causes is much more common than congenital or hereditary causes and includes testicular degeneration, orchitis, fibrosis and

calcification. (See Figures 180 through 190.) Lagerlof and others estimated that 75 to 80 percent of testicular pathology is related to testicular degeneration including fibrosis and orchitis. The epithelium of the seminiferous tubules is highly sensitive to any adverse influences with resulting marked effects on spermatogenesis. Testicular degeneration may be mild or severe and is usually bilateral as it is most commonly due to generalized disease processes. Unilateral degeneration can occur secondary to local testicular lesions such as tumors. Testicular degeneration may develop very rapidly within a few days or hours; while testicular regeneration proceeds slowly over weeks and months. If the basal layers of the germinal epithelium including the spermatogonia and Sertoli cells are destroyed regeneration of the germinal epithelium is not possible and the animals remain sterile. The pattern and signs of testicular degeneration are about the same despite the species or the etiologic factor(s) involved. In all cases degenerative changes in the mechanism of cell division or centrosomes are present in the primary spermatocytes and are responsible for reduced motility and increased numbers of pathologic spermatozoa with an abnormal morphology. Sperm cell numbers and concentration are decreased depending on the degree of degeneration of the seminiferous tubules. In severe disturbances of spermatogenesis, spermatocytes with restitution nuclei, with double the normal number of chromosomes as well as pyknotic nuclei are present in the ejaculate.¹⁷ Testes with degeneration of the seminiferous tubules are usually atrophic, softer and smaller than normal testes. In chronic cases the testicle may be firm due to fibrosis; even calcium may be deposited especially in the areas just peripheral to the rete testis. Histologically it may be difficult to distinguish between slight degrees of testicular degeneration and hypoplasia. Hypoplastic testes have a predisposition to degeneration.

Setchell²⁸ has described the natural and induced disfunctions of the testes in man and animals and has provided an extensive bibliography covering the testicular effects of radiation, heat, cold, nutrient supply, chemical and immunological damage, chromosomal, hormonal, viral, neoplastic and miscellaneous disease factors on the testes.²⁸

Causes of Testicular Degeneration include:

Thermal influences associated with elevation of the testicular temperature such as: cryptorchid and ectopic testes; inguinal hernias; (See Figure 180 and 181) scrotal dermatitis due to, irritants, choriopic mange in rams^{26a} and bulls (See Figure 182), myiasis in sheep, and lo-



Figure 182. Scrotal Dermatitis and Edema in a Bull Secondary to Chorioptic Mange. (Temporary testicular degeneration and infertility resulted that lasted for 2 to 3 months.)

calized skin infections, pox lesions or wounds; contusions and hematomas of the scrotum and testes; prolonged elevated body temperature as in certain infectious diseases and in prolonged high environmental temperatures, particularly associated with high humidity. Testicular degeneration is most common in tropical climates and involving breeds originating in the temperate zones.³ "Summer" infertility in bulls in the temperate zone is usually an individual bull problem. As many as 20 to 30 percent of bulls in a midwestern AI stud required air conditioning to maintain production of high quality semen during summer months when the ambient temperature and humidity are high. Direct heating of the scrotum may also be involved.²² Bulls were exposed to heat stress for 8 hours a day for 7 days; this resulted in a deleterious effect on semen quality reaching its peak at 2 to 3 weeks after the stress with recovery by 9 weeks.¹⁶ Rams maintained at ambient temperatures of 90° F. or above develop a marked drop in semen quality with about 10 percent motility and 70 percent abnormal sperm cells within a few weeks.^{4,8a,24} Recovery was not complete until 2 to 3 months after normal temperatures were restored. Shearing rams, especially their scrotums, monthly during the summer months greatly improved conception rate and embryo survival.¹² High ambient temperatures will also cause lowered fertility due to testicular degeneration

in boars.^{29,31} Heat primarily affects the spermatocytes but usually does not affect the spermatogonia, elongated spermatids or epididymal spermatozoa in the bull.²⁷ Heat has no effect on the Leydig cells. Even 10 to 20 hours insulation of the scrotum with a plastic bag that raised the skin temperature to 35° C had a definite depressing effect on semen quality that lasted for 3 to 9 weeks with a return to normal semen quality by 13 weeks.²⁷ Lagerlof¹⁹ carried out early classical experiments demonstrating that overheating or insulation of the scrotum of bulls caused rapid testicular degeneration and when normal scrotal temperature was restored, recovery was slow. Males that lie down for long periods of time such as bulls with bovine spastic syndrome, or males that are unable to rise, often develop testicular degeneration and atrophy due to the prolonged elevation of testicular temperature from the testes being held close to the body. When the scrotal temperature of bulls was raised to 38.4° C or 0.3° C below body temperature, the motility and percent of live spermatozoa in the semen decreased to zero by the second week.^{8b} After normal scrotal temperature was restored 11 weeks elapsed before motile cells were observed and 18 weeks were required for the recovery of normal semen quality. Application of an irritating ointment to the scrotum of boars resulted in increased heat to the area with testicular degeneration that was characterized initially with many immature sperm cells with a protoplasmic droplet followed by an increase in morphologically abnormal spermatozoa as the condition advanced.¹⁰

Colorado workers⁶ have reported on the damage to spermatogenic function induced in range beef bulls by low temperature down to -25° F. associated with winds of 60 miles per hour causing frostbite, necrosis of skin, scrotal dermatitis, heat, swelling, testicular degeneration and adhesions. Older bulls with pendulous scrotums were most seriously affected. The severity of the after effects were related to the amount of adhesions produced. Bulls provided proper wind shelter and dry bedding were not affected by such temperatures and wind. Scrotal frostbite resulting in infertility was reported in boars in Minnesota.² Scrotal dermatitis in dogs or other males due to any cause may result in testicular degeneration due to the elevation of the temperature of the testes.^{19b} This is favored by mild degrees of testicular hypoplasia. The presence of excessive fat in the inguinal region probably has little effect on the thermoregulatory mechanisms of the scrotum and testes unless short spermatic cords or other defects in the testes are present. The author has observed several bovine cases of mild scrotal hydrocele of unknown etiology where semen quality was not significantly affected. A severe chronic hydrocele resulting

in poor semen quality in a 3 year old bull was described. The bull responded to unilateral castration with a return to normal fertility 3 months after the operation.¹¹ A hydrocele secondary to a tumor of the tunica vaginalis was described in a dog.²⁵

Vascular lesions of the testes—Interference with the circulation and infarction of the testis can be produced by manual **torsion of the testis** or by the emasculator used for castration of lambs or calves. Congestion and pain of the scrotal testis due to naturally-occurring torsion or contusion has been reported in racing stallions, particularly Standard-bred trotters. With vigorous exercise these animals would start to spraddle their rear legs, become lame and then change from a trotting to a pacing gait. Affected Thoroughbred stallions would race normally for nearly one-half mile and develop an altered "hopping" gait. The testes would be swollen, congested and painful for the next 3 to 4 days. Dogs with inguinal or abdominal cryptorchid tests may occasionally develop torsion of the testis with a sudden onset of pain and associated symptoms. The author has observed one case of testicular torsion in a cryptorchid pig. Hemorrhagic infarction of the testis may follow torsion. Tumors of the abdominal testes may also predispose to torsion.

Testicular biopsies, particularly in bulls, often result in focal areas of testicular necrosis because of vessel damage when a desirable size of testicular material is obtained.²⁶ For this reason a technique of aspiration biopsy in bulls for cytologic but not for histologic studies was recommended.^{17,18} Testicular biopsies are more easily and safely done in the stallion and other animals.^{1,14} Testicular biopsies, even with a biopsy needle, may occasionally cause a degree or area of testicular degeneration due to interruption of the blood supply. In one study in dogs in which 28 biopsies were performed, one resulted in unilateral testicular degeneration and atrophy.¹⁴

Inflammation of the testicular artery in the horse may be caused by strongyle larvae, the equine arteritis virus and other unknown agents. This may produce areas of testicular degeneration.²⁰ Strongyle larvae can produce adhesions between the testis and its tunics. Age-associated vascular lesions such as hyaline degeneration in older bulls, rams and dogs may cause degenerative changes in the seminiferous tubules.²⁰ Suspensories of any type whether solid or mesh should not be used in shipping male animals. They have not proven necessary. The solid type might result in over-heating of the testes and both types might become maladjusted and cause pressure on the spermatic cord and affect testicular circulation.⁷

Varicocele is seen occasionally in the internal spermatic vein of rams and stallions but not bucks. (See Fig-

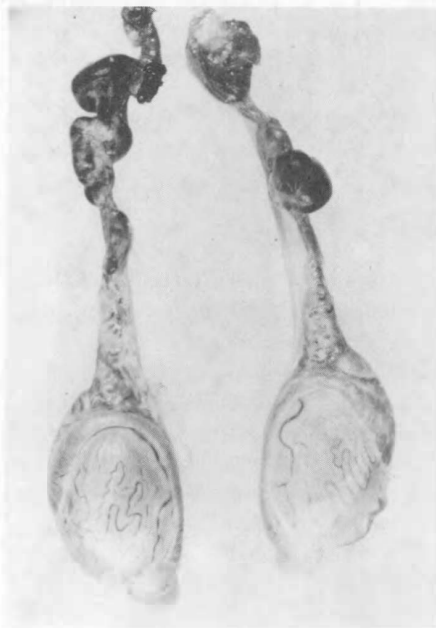


Figure 183. Varicoceles or Thrombosis of the Spermatic Vein in a Ram. (Courtesy K. McEntee.)

ure 183.) As in man the adverse effects on semen quality especially motility are probably slight to moderate.^{5,15,21,28} A severe case of infertility due to bilateral varicoceles in a 4-year-old ram with a high percentage of abnormal acrosomes along with other spermatozoal abnormalities and degeneration of the seminiferous epithelium was reported.²³ Varicocele may effect both the circulation of blood and the heat regulatory mechanism of the pampiniform plexus. Varicoceles may be palpated in rams.¹⁵ In a recent review^{15b} of varicoceles in rams it was proposed that this condition was caused by excessive venous pressure in the internal spermatic vein possibly due to arterio-venous shunts. The condition develops slowly over several years so it is usually seen in older rams. The incidence is low. In severe cases the varicocele may reach a size of 7 to 15 cm. and cause immobility, reduced libido as well as testicular degeneration, and infertility secondary to hypoxia of the seminiferous tubules. In large varicoceles a laminated thrombosis may be present. Affected rams should be culled as no cure is available and the condition might be hereditary.^{15b}

Irradiation, as other causes of degeneration of the testes, produces interference with spermatogenesis by injuring spermatogonia, spermatocytes and spermatids. The spermatocytes are most sensitive to irradiation while Leydig and Sertoli cells are quite resistant. The amount

of irradiation and length of treatment are highly important in the degree of effects produced and the rate of recovery. The first change in the semen noted was abnormal sperm cells about the sixth week after exposure of bulls to 100 to 400 roentgens.¹² A decrease in sperm cell numbers occurred by the eighth week and these numbers did not begin to return to a normal level until 15 weeks. All bulls had reached nearly normal levels by 24 weeks after exposure. Bulls given doses totalling 600 to 1100 roentgens, developed aspermia by 16 weeks, remained aspermic for 10 weeks and fairly good recovery had occurred by 12 to 24 months.^{13,14}

Hormonal causes—Testicular degeneration and atrophy of the testes occurs in the dog and rarely in other animals due to tumors of the anterior pituitary gland or hypothalamus interfering with the production of gonadotropic hormones. This is called **dystrophia adiposogenitalis syndrome** in dogs.^{8b} Besides testicular atrophy, obesity and other signs commonly develop. Excessive estrogenic hormone produced by Sertoli cell tumors and testosterone, and rarely estrogens, produced by Leydig cell tumors may suppress FSH and LH production and cause testicular degeneration. In the past (1950's) infertile men with oligospermia were treated with large doses of testosterone for a prolonged period to completely suppress spermatogenesis. Following this treatment a "rebound phenomena" was reported in which higher than normal concentrations and numbers of spermatozoa were produced. In summarizing this data only 7.5 percent of 840 men treated showed any significant improvement.³ Prolonged doses of testosterone, estrogens or anabolic steroids should not be given to male animals.¹¹ (See Hormonal Causes of Infertility in Males.)

Age Effects—McEntee¹⁰ stated "Permanent and progressive testicular degeneration occurs fairly frequently in all species without any indication of its pathogenesis." Senile atrophy of the testes is common in dogs over 10 years of age and in cats over 12 years of age.¹ A decline in fertility in bulls as they became older has been reported.^{4,5} Vibriosis might have been present as a factor in the latter report. A decline in fertility of 0.31 to 0.51 percent per year in over 150 bulls used in artificial insemination as measured by nonreturn rates was reported.⁷ Aged bulls, 7 to 13 years old had a lower sperm cell output per ejaculate than young bulls, 2 to 6 years old, 7 billion and 10 billion, respectively.⁷ Aged bulls had 10 percent fewer morphologically normal spermatozoa and the motility rate was lower. Degeneration of the testes based on semen examinations in aging stallions was similarly described.⁹ The author has observed that older bulls after they reach 8 to 10 years of age may develop testicular degeneration fairly rapidly at any time.

It is an uncommon bull that produces good quality fertile semen up to 15 or more years of age. Many disease, genetic and management factors influence this age effect.

Subacute or acute trauma, stress, or disease may cause rapid or progressive testicular degeneration in males. Those that have been associated with reduced fertility and a decline in semen quality are: shipping under adverse conditions of heat and cold, severe fatigue, excessive physical work, traumatic gastritis in bulls,⁶ liver or abdominal abscesses, multiple severe contusions with fractured ribs as would occur in a fight between bulls, severe arthritis, severe myiasis or "fly strikes" in rams, severe screw-worm infestations, moderate to severe foot rot in rams, suppurative arthritis and severe quitters in bulls, acute laminitis in rams, horses and possibly other species, buckshot wounds especially of the scrotum and testes, kick wounds and resulting hematomas of the testes and scrotum in stallions, and extensive infected wounds. Good care and management will do much toward avoiding testicular degeneration due to these causes. Although Polish workers⁸ reported a temporary reduction in fertility for about three months after shipping 29 bulls from Holland to Poland, 60 bulls, used for artificial insemination, moved 300 to 2000 miles in the U.S. without a suspensory and no reduction in semen quality was noted in the months following shipment.¹⁵

Acute or chronic, localized or systemic infectious diseases are common causes of testicular degeneration with moderately to severely reduced fertility in males. Infections producing orchitis or epididymitis have a direct effect on the testes due to the inflammatory reaction causing heat, edema, congestion, circulatory interference, ischemia and even infarction due to the thick firm tunica albuginea that restricts normal swelling of the testicular parenchyma. In bacterial diseases localizing in the testes, abscessation may occur. (See Figures 184 and 185.) Infectious agents resulting in orchitis are: **Brucella abortus**, both field strains and Strain 19 in bulls;¹⁷ **Brucella suis** in boars; miliary or chronic tubercular infectious with **Mycobacterium tuberculosis** of the testes in bulls and boars; **Corynebacterium pyogenes**, usually carried to the testes by the blood from primary infectious sites in bulls and rams; **Actinomyces bovis** in bulls,¹⁴ **Malleomyces mallei** (glanders organism) in horses; **Salmonella abortus equi** and "epizootic cellulitis" due to the arteritis and the **influenza viruses** in horses; **Corynebacterium ovis** and **Pasteurella pseudotuberculosis** in rams; lumpy skin disease in cattle; sheep pox virus in rams;¹⁹ an enteric virus, possibly IBR-IPV virus, that markedly affected the spermatocytes and caused arrested spermatogenesis in bulls has been described in

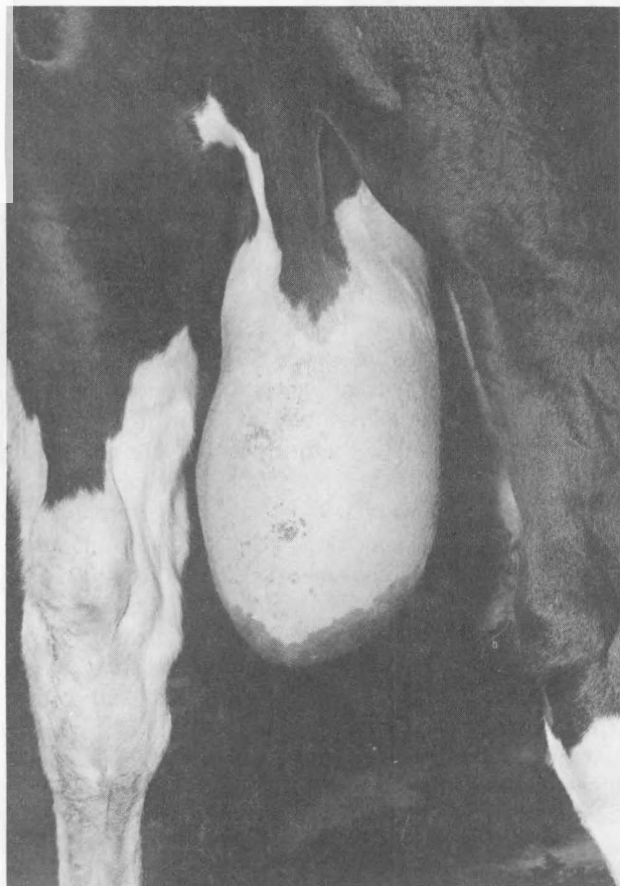


Figure 184. Acute Orchitis of the Right Testis in a Holstein Bull.

Belgium.^{1,2} These workers^{1,2,10} reported on a G-UP virus isolated from the genital organs of bulls that caused infertility and an abnormal sperm picture, degeneration of the seminiferous epithelium, ulcers in the mouth, stiff gait, anorexia and other lesions highly suggestive of foot and mouth disease. A more chronic virus orchitis of bulls has been reported in Czechoslovakia.²¹ Other possible related viruses may cause orchitis in bulls.¹² The IBR-IPR virus when injected into susceptible bulls may cause a severe and rapid degeneration of the seminiferous epithelium and sterility.^{26,29} Most bulls recovered and were fertile in about 3 months. During the height of the degeneration only Sertoli cells and spermatogonia lined the seminiferous tubules. A few bulls developed an edema of the scrotum and fibrous adhesions occurred around the testes and spermatic cord.

Canine distemper affecting sexually mature dogs may cause a mild orchitis and testicular degeneration as well as an epididymitis.^{5,19} *Brucella canis* in dogs caused

scrotal swelling and dermatitis, orchitis, fibrosis, atrophy and sterility.^{5,6,7a,11,22} After oral inoculation of dogs with *Br. canis* 20 to 80 percent of the sperm cells were abnormal, including swollen midpieces and distal protoplasmic droplets within 3 to 4 weeks after the inoculation. By 8 weeks nearly all spermatozoa exhibited marked defects generally attributed to the epididymitis and seminiferous tubule degeneration.¹¹ (See Abortion and Epididymitis due to *Brucella canis*.) Any acute or subacute epididymitis would reduce fertility both because of the inflammatory reaction and heat produced as well as by obstructive lesions in the epididymal tube. (See Epididymitis due to *Brucella ovis*.) The probable viral disease of specific bovine venereal epididymitis and vaginitis, "epivag," also causes an orchitis with testicular degeneration and atrophy.³ A mycoplasma was isolated from three ovine cases of orchitis,²⁰ and *Mycoplasma hyorhinis* infection in swine often results in swelling of the scrotum and adhesions between the testes and the tunics.²⁸ *Chlamydia psittaci* may cause orchitis as well as polyarthritis in rams.²³ This organism was recovered from two other cases of orchitis in rams.⁸ A seminal vesiculitis syndrome in bulls characterized by seminal vesiculitis, epididymitis and orchitis was described by Colorado workers²⁷ from which they re-

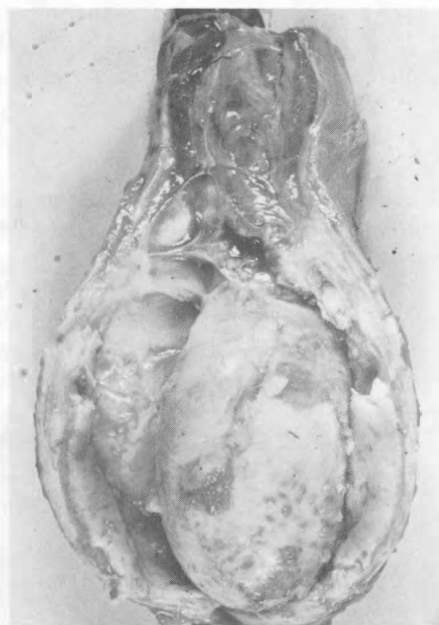


Figure 185. Acute Orchitis and Periorchitis Secondary to a *C. pyogenes* Infection. (After unilateral castration and a 6 to 8 month rest period this bull (Figs. 184 and 185) recovered and was fertile for over 3 years.)



Figure 186. Longitudinal Section of a Normal Bovine Testis (Note the bulging and the uniform color and texture of the parenchyma) (Courtesy K. McEntee).

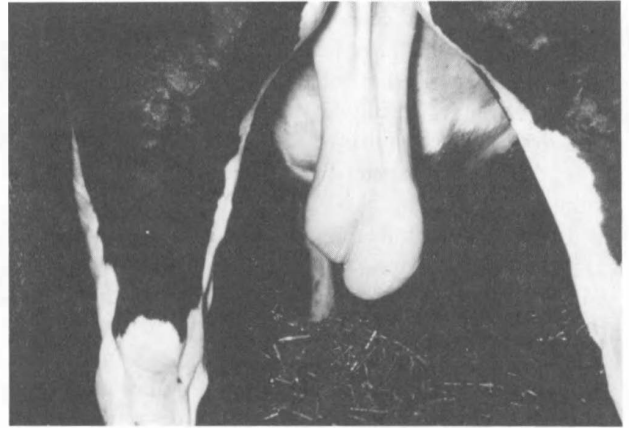


Figure 188. Advanced Testicular Degeneration, Fibrosis and Atrophy, Especially of the Left Testis.

covered a chlamydial agent. *Nocardia farcinica* in bulls,³ and *Besnoitia besnoiti* have been occasionally reported as a cause for orchitis in bulls.^{7b,16,24} Severe obstructive lesions such as sperm granulomas affecting the efferent ducts may cause a back pressure from the spermatozoa and the testicular secretions resulting in testicular degeneration. (See Figure 189.) The affected testes may be somewhat enlarged.¹⁹ Sporadic infections of the testis with



Figure 187. Testis with Advanced Testicular Degeneration, Fibrosis and Calcification (Courtesy K. McEntee).

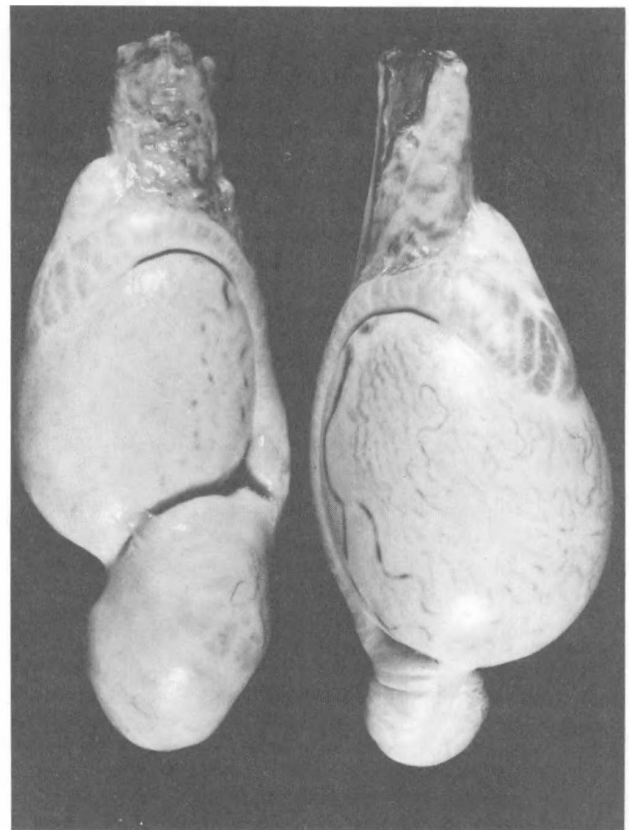


Figure 189. Fibrosis and Sperm Granuloma of the Tail of the Epididymis of the Left Testis in a Ram due to *Br. ovis*. (Note the moderate atrophy of the left testis compared to the normal right testis.) (Courtesy P. C. Kennedy.)

staphylococci, streptococci, *E. coli*, *Proteus* and *Pseudomonas* organisms have been reported as a cause of orchitis in dogs and other male domestic animals.²⁵ Erythematous lesions of horses resulted in edema of the legs, sheath and scrotum and orchitis with secondary testicular atrophy.¹³ During the acute disease inclusion bodies were commonly observed in the leucocytes. This disease should be differentiated from equine infectious anemia, piroplasmiasis and dourine.

Infectious diseases of a systemic nature that cause testicular degeneration and lower fertility temporarily due to the accompanying high fever include: pneumonia and shipping fever, possibly IBR-IPV, equine infectious anemia, actinobacillosis, strangles, blue-tongue virus vaccination,⁹ and tick-borne fever infection in rams.³⁰ (See Figure 190.) Pseudorabies in swine had no effect on semen quality or fertility unless severe clinical signs developed.¹⁸ Those infectious diseases causing gradual debilitation, loss of weight and testicular degeneration with atrophy include: foot and mouth disease, actinomycosis, John's disease, pyelonephritis, chronic peritonitis, and lymphomatosis.

Nutritional factors related to testicular degeneration are usually those caused by severe underfeeding or starvation. (See Nutrition and Infertility in Males.) Diets for males sufficient for growth and maintenance are adequate for fertility. **Chronic disease states** associated with

inanition and debility and testicular atrophy may include: severe parasitisms, either external or internal such as: lice, mange, ticks, roundworms, flukes, and etc., senile changes due to worn or diseased teeth, chronic arthritis, tumors, fat necrosis around the large intestine in bulls, severe spastic syndrome and other possible diseases interfering with the intake and passage of food through the gut. Malnutrition may complicate these other chronic diseases. Improper care and management of bulls accustomed to special care and feeding may cause a marked loss in weight resulting in impotency and testicular degeneration and atrophy. This has been observed in several instances when a young fertile, but timid, bull was introduced into a new herd and permitted to run with the cows in a small, confined area. The cows would drive the bull away from the feeding racks causing the bull to become emaciated and sterile. Severe vitamin A deficiency characterized by night blindness, lacrimation and ophthalmia usually precedes testicular degeneration and poor semen quality. Under range conditions during drouths vitamin A deficiency usually is accompanied by protein and carbohydrate deficiencies. Malnutrition, debility and cachexia produce degeneration and atrophy of the seminiferous epithelium by causing a suppression of the release of gonadotropic hormones from the pituitary. Zinc deficiency may be associated with certain cases of infertility in animals.¹⁴

A high level of feeding and the accompanying obesity has no effect on semen quality in a normal male, but does effect their libido and willingness to breed. The author has observed a number of highly-conditioned beef show bulls producing semen of excellent quality. However, if obesity accompanies testicular hypoplasia, a short spermatic cord and much fat in the inguinal ring it does not follow that the obesity is the primary cause of the resulting infertility.

Poisons or toxins may adversely affect the germinal epithelium. Testicular degeneration in bulls and hyperkeratosis in rams was caused by ingestion of chlorinated naphthalenes.¹² Dipping of rams in arsenic solutions causes degeneration of the seminiferous tubules in sheep.⁷ Antimony compounds injected for the treatment of heartworms in dogs have been reported to cause temporary sterility.¹ There is no evidence that copper sulphate or phenothiazine used in worming sheep have harmful effects on the testes. There is no evidence that systemic organic phosphate insecticides affect semen quality in bulls.⁶ Severe prolonged toxemia and reduced semen quality lasting for 6 to 12 months resulted from using chlorpyrifos (Dursban 44) pour-on for the control of lice in AI bulls.⁴ This compound, which did not affect steers or cows, probably interacted in some manner with tes-

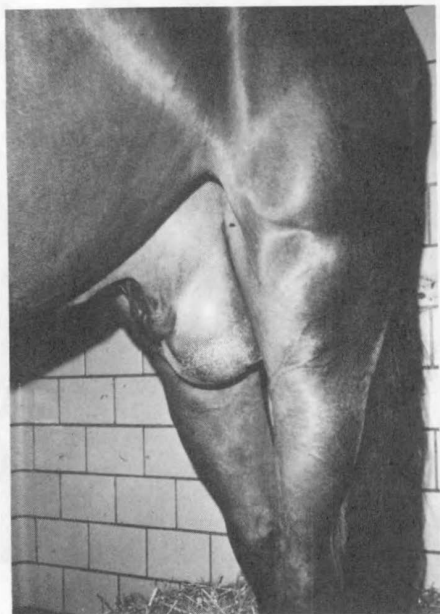


Figure 190. Edema of the Scrotum of A Standardbred Stallion, Associated with Equine Infectious Anemia.

tosterone to produce these effects.

Potassium nitrate also had no effect on semen production. The author has seen no ill effects from the use of sodium iodide for actinomycosis or actinobacillosis in bulls in artificial insemination studs. A number of chemical, metals and rare earth salts can produce degeneration of the seminiferous epithelium in a variety of species.¹¹ Setchell¹⁴ has cited many references on chemical compounds that affect testicular function including cadmium salts, other heavy metals, diesters of methane sulfonic acid, nitrofurans, halogenated compounds, alcohol and actinomycin D in animals and man.^{12,14}

Auto-immunization might play a role in a few cases of testicular degeneration. Degeneration has been produced experimentally in rams, bulls and laboratory animals by the subcutaneous injection of autologous testicular material together with Freund's adjuvant. Degeneration may occur with or without inflammation. No natural cases of testicular degeneration due to autoimmunization have been reported.^{2,9,10,12,13} Two reports have indicated that anti-LH serum or an anti-LH adjuvant product injected every 3 weeks in bull calves and ram lambs will induce testicular degeneration and sterility. This product immobilizes the male's own gonadotropic hormones and testosterone necessary for spermatogenesis. Lymphocytic thyroiditis, a possible genetic autoimmune disease of dogs, especially Cocker Spaniels, Corgis and Beagles, may also be associated with lymphocytic orchitis and infertility.^{8b}

Testicular Neoplasms. Testicular tumors are uncommon in most domestic animals except the dog and possibly old bulls. Primary testicular tumors are usually of three main types and originate from the interstitial cells,



Figure 191. Bilateral Interstitial Cell Tumors of a Testis in an Old Infertile Guernsey Bull. (Courtesy K. McEntee.)

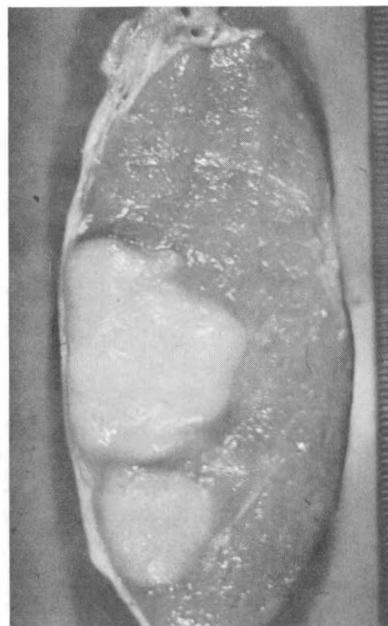


Figure 192. Sertoli Cell Tumor of the Testis of a Bull. (Courtesy K. McEntee.)

the Sertoli cells and the germinal epithelium. The increased incidence in dogs may be due to a genetic predisposition in dogs and to the maintenance of intact male dogs until they become senile. The incidence of tumors in cryptorchid or retained testes is high, especially in dogs, for the same reason. In the larger animals relatively few uncastrated males are kept until they reach an advanced age. Sperm cell production and fertility of bulls with testicular tumors over 1.0 cm. in diameter were significantly lower than in unaffected bulls or bulls with small tumors.⁶ Bulls with large interstitial tumors had 30 percent of their ejaculates discarded as unfit for use for artificial insemination while normal control bulls had only 2 percent of their ejaculates discarded. (See Figure 191.) Thus large tumors result in testicular degeneration probably due to the compressing effect of the tumor on the adjacent seminiferous tubules. The degeneration may also be due to the excess steroids produced by the interstitial, or Sertoli cell tumors.¹² (See Figure 192.) Lymphosarcoma of the testis of animals is rare.

In bulls testicular tumors are seldom observed except in old animals. Interstitial cell tumors of a benign type are occasionally observed in bulls over 7 to 10 years of age. These may be multiple and in some cases they are large enough to be palpable as small, round, masses, liver-like in consistency, and causing the testes to feel lumpy on palpation. Interstitial cell tumors were found

in 19 percent of 52 Guernsey bulls.⁶ This was significantly higher than the 6 percent incidence in 164 bulls of the other breeds. An interstitial cell tumor in a testis of a 3-month-old calf was described.⁹ This type of tumor usually has a deep ochre or orange-brown color with a homogeneous, glassy consistency resembling a corpus luteum.¹² (See Figure 191.) An adenocarcinoma, seminomas and several Sertoli cell tumors have been described in bulls. (See Figure 192.) The benign interstitial cell tumors in old men, dogs and probably bulls may be related to a hormone imbalance.⁹ Small fibropapillomas or melanomas and varicose dilatations of scrotal veins occur in older bulls and are occasionally seen on the scrotal skin. These small varicose lesions on bulls' testes may be associated with improper temperature regulation of testes and infertility during the hot summer months.

In stallions testicular tumors have been described only occasionally. Uncommon dermoid cysts or teratomas of the testicle of the horse are most often found in cryptorchid testes.^{4a,b,13,24,28} They often contain large cystic structures and hair or bone. Forty-nine testicular tumors

of a total of 142 neoplasms were found in 77,000 slaughtered horses.⁹ Rare seminomas in stallions were described.^{9,10,13,26} The latter report described two equine seminomas that metastasized.

Only one testicular teratoma was found in 700 horses castrated at the New York State Veterinary College.¹² An adenocarcinoma in a retained testicle in a horse with metastasis to the lungs and mediastinum was described.⁹ Occasional interstitial cell tumors of the equine testis have been reported.^{12,23} In some of the cases the affected animals were extremely aggressive and vicious but after castration became gentle and quiet. Sertoli cell or sustentacular cell tumors in horses were rare.¹³ A melanoma of the scrotum has been observed in a stallion.⁷ Lipomas on the surface of the equine testis are not uncommon.¹²

In rams testicular tumors are rare. No large series of testes in old boars, rams, or cats has been examined.⁹

In boars testicular tumors are very unusual. A malignant tumor of an undescended testis in a boar was described.²⁸ A teratoma was observed in a cryptorchid porcine testis.⁴ A seven-year-old boar with a seminoma of a testis that was four times as large as the opposite testis was reported.⁸ When the boar was bred, about 250 ml. of semen was collected but no spermatozoa were present and on histologic section areas of necrosis were found in the tumor.

In cats testicular tumors apparently are rare. Several Sertoli cell tumors in this species have been reported.^{13,27}

In dogs testicular tumors are observed at any age but most commonly in dogs over five years old. There was a higher incidence of testicular tumors in dogs than in humans.⁹ An incidence of 16 percent of tumors in 580 unselected adult dogs was reported.⁵ The three principal testicular tumors in dogs are, seminomas, Sertoli cell tumors (tubular adenomas), and interstitial cell tumors.¹³ Their comparative incidence is noted in Table 25. Teratomas have not been recorded in canine testes.⁴ Most canine tumors are usually benign but up to 10 percent of the Sertoli cell tumors and a few seminomas may be malignant in character.^{5,17} Of 177 tumors in 85 dogs, 55 percent were multiple, 45 percent were bilateral and 35 percent of the dogs had two or more types of tumors.¹⁹ Five percent of all tumors developed in cryptorchid testes. There is a significant correlation of Sertoli cell tumors and seminomas with cryptorchidism in dogs, (See Cryptorchidism). The age of the affected dogs averaged 10 to 11 years but the range was 3 to 20 years. Dogs with affected cryptorchid testes were younger than dogs with affected scrotal testes.

In another survey of 198 dogs with testicular tumors, the numbers of seminomas, Sertoli-cell tumors, interstitial cell tumors and combinations of several types of tu-



Figure 193. Testicular Abscesses in a 3-Month-Old Calf.

Table 25. Summary of Reports on the Comparative Incidence of Testicular Tumors in Dogs

Tumors	Innes ⁹	Dow ⁵	Scully & Coffin ¹⁹	Mulligan ¹⁵	Totals	
					No.	Percent
Seminoma	32	45	55	14	146	35.3
Sertoli cell	15	36	33	13	95	23.5
Interstitial cell	14	56	88	12	170	41.1

mors were 47, 46, 67 and 38, respectively. Concomitant clinical changes with each type of tumor was reviewed.¹¹ In a large cohort study the incidence of testicular neoplasms in cryptorchid dogs over 6 years of age was 68.1/1000 dog-years at risk. The incidence of Sertoli cell tumors and seminoma was twice as high in dogs with unilaterally retained inguinal testicles as in abdominal cryptorchids.¹⁸

Seminomas are noted in old dogs over 7 years of age and arise from the germinal epithelium of the seminiferous tubules.¹³ These tumors originate in atrophic seminiferous epithelium and the tumor is intratubular before becoming diffuse.¹⁹ These tumors grow slowly for months but may develop rapidly at any time. They are rather soft in consistency and hemorrhage or necrosis may be present. On section they appear dull-white or gray in color. Affected dogs may exhibit lameness and pain by crouching and hunching. Seminomas were frequently bilateral and occasionally metastasized to the regional lymph nodes.^{11,12,19,22} A seminoma in an abdominally located testis was removed. Nine months later a large metastatic tumor of the abdominal cavity was diagnosed.²² In some cases seminomas and interstitial cell tumors are present together in the testis.

Sertoli cell tumors, or tubular adenomas are possibly the least common of the principal tumors of the canine testis. This tumor arises from the Sertoli or nurse cell of the seminiferous tubules and is usually seen in older dogs. The tumor is often characterized by marked feminization of the male by the estrogens secreted by the tumor cells.³ Recent studies indicated that the estrogenic substances produced by the tumor and causing feminization of the male were not the usual estrogens found in animals.²¹ The dog may attract other males. The penile sheath is swollen. There is a definite loss of hair, especially on the abdomen and lower parts of the body, and a loss of sexual desire. Mammary hypertrophy or gynecomastia, and enlargement of the nipples and in some cases development of mammary tumors may occur. Atrophy of the testicular tissues and penis develops. Pigmentation of the abdominal skin and scrotum and female distri-

bution of body fat are exhibited. The prostate may undergo marked enlargement due to squamous metaplasia and cysts; or it may become markedly involuted due to atrophy of the epithelial elements and collapse of the acini.¹⁹ Bone marrow hypoplasia due to endogenous estrogen myelotoxicosis from Sertoli cell tumors were reported in eight dogs, five of which died due to hemorrhage with thrombocytopenia, anemia and infection and fever associated with granulocytopenia.²⁰ These tumors are rather large in size, firm, nodular, and fibrous on palpation. Rarely a large hydrocele may be associated with Sertoli cell tumors, especially those that metastasize. On cross section Sertoli-cell tumors are pale-yellow or grey in color and may contain necrotic, cystic, or hemorrhagic foci. If no metastases have occurred recovery from the above dramatic symptoms takes place promptly after the affected testis is removed.

Interstitial-cell tumor, adenoma, or Leydig-cell tumor is the most common tumor in old dogs. Although this tumor is present in many old dogs, it is of little clinical significance. Most of them are found only at autopsy. They are often overlooked because of their small size; 1 mm. to 2 cm. is their usual size.¹² Although 41.1 percent of testicular tumors cited in Table 25 were of the interstitial cell type, this percentage might well have been higher if all the small interstitial cell tumors had been found and recorded. Careful work in one study showed that 50 percent of testicular tumors were of the interstitial cell type.¹⁹ Nodular hyperplasia of the interstitial cells is seen commonly in older dogs with senile testicular atrophy. Nodular hyperplasia is probably a preneoplastic change but the division between nodular hyperplasia and interstitial cell tumor is arbitrary.¹² These tumors probably produce androgens because the prostate in affected dogs is normal or hypertrophied. In uncommon instances these interstitial cell tumors may produce estrogenic compounds resulting in male feminizing syndrome with alopecia, atrophy of the prepuce and gynecomastia.¹⁴ The tumors consist of single or multiple well-circumscribed nodules, brownish-orange in color and soft in consistency. Large tumors may occasionally be palpated in the testes of old dogs. They are similar in appearance to a corpus luteum and are likely to be bilateral and often contain hemorrhagic and necrotic foci. This condition probably is nodular hyperplasia of the interstitial cells and possibly these nodules should not be called true tumors.⁹ Although two cases in which this tumor metastasized have been described, metastasis is rare.⁹

Melanomas and mast cell tumors are not uncommon in the scrotal skin of the dog. The latter are usually malignant.² A scrotal hemangioma in a dog resulted in fatal hemorrhage.²⁵ Canine tumors should be carefully differ-

entiated from orchitis or epididymitis, traumatic swellings or hydrocele. The latter condition may be either congenital or secondary to orchitis. Canine perianal gland tumors are probably androgen-dependent tumors that can be arrested by castration.¹⁶ About 85 percent occur in older male dogs with a definite breed incidence in Cocker Spaniels.

Genetic hereditary influence on acquired testicular degeneration have been reported in identical twin bulls.¹ Genetic constitution appeared to influence the onset of generalized arthritis, fat necrosis, traumatic gastritis, and associated testicular degeneration in identical twin bulls. The increased predisposition and earlier occurrence of testicular degeneration in bulls with some testicular hypoplasia was noted.¹² Certain bulls may be more resistant to testicular degeneration than other bulls when affected by similar etiologic agents. Thus the genetic constitution of each male and his seminiferous epithelium and their resistance or ability to withstand adverse influences must be considered in the etiology and signs of testicular degeneration.

The signs of testicular degeneration are similar in all species of animals despite the etiologic factor(s) involved. The signs vary in degree from mild to severe depending upon the cause and duration of the degeneration.

The fertility of the male may range from only slightly reduced conception rates, to moderate to severe infertility, to complete sterility.

The age of the male with testicular degeneration may vary from young to old with most cases in the older animals.

The size of the testes is usually reduced from normal to about one-half to two-thirds normal size depending on the duration and degree of degeneration and atrophy of the seminiferous tubular epithelium. Since 77.1, 72.2 and 49.9 percent of the testicular volume is comprised of seminiferous tubules in 2.5-year-old, adult, and one and one-half-year-old bulls¹ the close association of the degree of testicular degeneration and testicular size is apparent. In acute orchitis, other inflammatory conditions, obstruction of the efferent ducts, or testicular tumors, an increase in testicular size is often noted.

The consistency of the testes is soft and flabby in acute, moderate to severe testicular degeneration. This is understandable since about 70 percent of the volume of the testis is composed of seminiferous tubules and their contents. In mild testicular degeneration consistency differs only slightly from an elastic, tonic, slightly tense, fluctuating normal consistency. In these cases comparing the testicular consistency of the bull in question with several normal bulls of the same age may be helpful.

The use of a tonometer has proven of value in the objective measurement of testicular consistency.^{4,5} In 150 bulls in an AI stud, soft, medium and firm consistencies of the testes were found in 14, 30 and 56 percent, respectively. Bulls with soft testes tended to produce fewer sperm cells. The tonometer test correlated closely with other tests of semen quality.

Acute orchitis is characterized by a tense swelling and enlargement of the testis accompanied by pain and heat. This should be differentiated from hydrocele or hematocele. Chronic degeneration and atrophy of the testes especially in older males whether following severe acute or chronic diseases is characterized by fibrosis of the testes often with calcification. The latter is impossible to palpate but about 25 percent of 158 bovine testes from abattoir material revealed calcification on radiographic examination.² Fibrotic testes are hard, firm and often lack tonicity or elasticity. Ultrasonics can be of value in the detection of connective tissue in fibrosis of the testes.⁴ Testes containing tumors may be enlarged and have an irregular shape and consistency on palpation.

The libido or sex drive is usually not related or associated with testicular degeneration except in acute orchitis or other painful testicular diseases or in testicular atrophy associated with severe debility or inanition due to a variety of causes. As indicated previously the Leydig-cells are much more resistant to stress factors than the cells of the germinal epithelium.

The semen examination is very helpful in diagnosing testicular degeneration. Semen may be collected by the artificial vagina, by electroejaculation or other methods as will be described later. The former method is preferred. Since it requires about 50 to 60 days or more for sperm cells to develop from spermatogonia until they are ejaculated, it may be desirable in diagnosing testicular degeneration to take several samples at weekly or greater intervals. The semen production and quality in young immature bulls continues to improve in motility, concentration and morphology for months after puberty is reached. So if an initial semen sample is poor, subsequent samples are indicated. The first semen samples taken after a long period of sexual rest may also be misleading as these are often of poor quality with many dead or aging spermatozoa with acrosomal degeneration. In males in which testicular degeneration is severe, semen quality is usually poor.

Sperm cell concentration may be reduced to one-third to one-half of normal values or show severe oligospermia or azoospermia. Watery, translucent semen is common in severely affected bulls and rams.

Sperm cell motility is reduced one-third to one-half or more due to an increase in abnormal cells, dead cells,

(necropermia), or poorly viable defective cells. The duration of motility after ejaculation is shortened.

Sperm cell morphology after staining reveals an increase in dead spermatozoa and abnormal heads, tails, and middle pieces. The degree of change in the morphology of cells may vary from normal semen which usually contains from 5 to 15 percent abnormal cells, to a 15 to 20 percent increase in abnormal cells in mild cases of testicular degeneration, to a 20 to 30 percent increase in moderate testicular degeneration, and to a 35 to 60 percent or greater increase in severe testicular degeneration. The occurrence of large numbers of spermatozoa with primary abnormalities that arise during spermatocytogenesis or spermatogenesis and early spermiogenesis are more indicative of a severe testicular degeneration than the presence of secondary abnormalities that occur later in spermiogenesis or during passage and storage of spermatozoa in the epididymis.^{3,7,8} (See Semen Examination.) The appearance of primitive cells such as giant cells and spermatocytes with restitution or pyknotic nuclei together with a marked reduction in sperm cell concentration and motility are signs of severe degeneration of the testes.

Other tests for viability and longevity may be employed but are more difficult to perform and do not add greatly to the information obtained by the previous tests. The volume of the ejaculate is not related to the degree of testicular degeneration since most the ejaculate comes from the secretions of the accessory glands. Testicular biopsies may be of value in certain species such as the dog and stallion, but are impractical for technical reasons in the bull.⁸ Furthermore the above signs and additional tests of sequential semen samples will accurately reveal the relative degree of progression and regression of testicular degeneration.

Prognosis—The prognosis in testicular degeneration is variable depending upon the causative factors, the duration and degree of the degeneration, and the age and value of the male. Although testicular degeneration can occur rapidly within a few hours, days or a week or more, recovery is very slow usually requiring 3 to 6 months or more in moderate to severe cases. The prognosis in slight or mild cases of testicular degeneration in young or middle-aged bulls due to transient and correctable causes is fair to good. Controlled breeding during the recovery period may result in fair to good fertility in some males.

The prognosis is guarded to fair in young males with only moderate evidence of testicular degeneration; and in older males suddenly developing infertility due to a transient disease where advanced testicular changes do not occur, such as in; mild cases of trauma to the testes, scrotal inflammations, toxemia or poisonings, mild ex-

posure to irradiation, chronic but curable systemic diseases causing debility, and inanition due to semistarvation.

The prognosis is poor in progressive senile testicular degeneration, in acute severe orchitis especially if it is bilateral and associated with abscessation, in advanced fibrosis and atrophy of the testes, in degeneration associated with hypoplasia in young to middle-aged males, and in older males with bilateral tumors of the testes.

Once the testes have been severely damaged regeneration can never be complete. If severe secondary infections or lesions occur in the epididymides, accessory glands, or vasa deferentia the prognosis is also guarded to poor.

The **treatment** of testicular degeneration requires the correction or the alleviation of the causative factor(s). Sexual rest is usually advised, since in most cases fertility is reduced to a point where the use of the male is questionable. Males with mild degrees of degeneration not severely influencing fertility should be used sparingly so as to maintain as large a number as possible of normal, motile spermatozoa in each ejaculate. A balanced ration high in vitamin A and a good quality and variety of protein are indicated. Good-quality roughage or pasture is highly desirable. Some exercise especially on pasture is usually recommended for the larger farm animals, although it has been shown that forced exercise has no effect on the fertility of the bull.⁹ If excessive heat and humidity is the cause of the temporary infertility in bulls, air conditioning or cooling is indicated.

Hormones are of no proven value. Testosterone, various FSH products, and thyroxine have been tried but none have any demonstrated effect in the therapy of testicular degeneration or hypoplasia. Plasma concentrations of these hormones are usually normal or elevated in affected males. Furthermore the gonadotropic hormones to be of any value must be given over a period of a month or more and should be prepared from biologic sources from the same species to prevent antihormones from developing. Many studies have reported on the uniformly poor results from the hormonal or dietetic therapy of testicular degeneration in men.^{6,10,12}

In acute orchitis, sexual rest is imperative. Physical rest is usually advisable and can be provided by close confinement of the male. In the early acute stages heavy parenteral broad-range antibiotic therapy is indicated. Glucocorticoid or non-steroidal anti-inflammatory agents along with the antibiotics might be helpful in reducing the inflammatory reaction. Ice packs should be applied to the testes by a suitable sling or bag fixed between the legs and tied over the back. This therapy should be continued until the acute, severe symptoms have subsided.

When the orchitis is unilateral and severe or incurable, removal of the affected testis may hasten recovery or save the breeding life of a valuable male. The testis should be examined carefully and cultured after removal to detect the responsible agent so that suitable precautions can then be taken for the future use of the sire if his fertility returns. The Brucella-infected bull or boar should not be used either artificially or naturally in a Brucella-free herd. Heat or a mild counter-irritant ointment to the inflamed testis and swollen scrotum should never be used. The preferred treatment for testicular tumors is prompt castration or removal of the affected testis. If metastases have occurred, symptoms caused by the secondary tumors will usually develop within a few months. Cryptorchid testes should be removed while the affected males are still young to prevent the occurrence of tumors or abdominal complications common in these structures in later life.

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Pathological or Functional Disturbances of the Epididymis, Ductus Deferens and Accessory Reproductive Glands in the Male Causing Failure of Fertilization or Conception.

Pathology of the Epididymis—Disease of the epididymis includes: infection of the epididymal duct and epididymitis, anomalies causing sperm granulomas, tumors, and functional or hormonal disturbances.

Epididymitis, or inflammation of the epididymis, is occasionally observed as an acquired lesion in all species of animals and is caused by or may be secondary to the same factors causing orchitis. Infectious causes of epididymitis most commonly involve the tail of the epididymis but may involve the body and head of the epididymis. These include: ***Brucella abortus*** in bulls, ***Brucella suis*** in boars, ***Brucella ovis*** and ***Actinobacillus seminis***^{23,30} in rams, ***Brucella canis*** in dogs,¹² ***Streptococcus zooepidemicus*** in the stallion,⁵¹ ***C. pyogenes*** and other miscellaneous organisms such as streptococci, staphylococci, *Proteus*, *E. coli*, ***C. pseudotuberculosis***, ***Pseudomonas aeruginosa*** and ***Mycoplasma bovis-genitalium***.⁴³ Infections may be caused by organisms, such as mycoplasma or possibly ureaplasma invading the epididymis through the ductus deferens or by way of the blood or lymph vessels. (See seminovesiculitis.) Traumatic injuries may also produce an epididymitis.⁴⁵ Canine distemper virus in sexually mature dogs causes an epididymitis.³⁷

A specific bovine venereal epididymitis and vaginitis or "epivag" has been described in Chapter XIII. This venereal and probably viral disease, found only in East, South, and Central Africa, is usually characterized in the bull by a marked bilateral hardening and swelling of the tail of the epididymis and sterility. Pathological fibrotic changes also occur in the ductus deferens, testes, and vesicular glands.^{9,32} There is no cure for affected males

but artificial insemination has been an effective control measure to prevent the spread of this venereal disease. Other diseases of the testis and epididymis of bulls in South Africa have been described.⁵³ ***Besnoitia besnoiti*** produces elephantiasis of the scrotal skin and cysts in the scrotum, inguinal canal, testes, and epididymis. These cysts may persist and calcify, causing sterility.

Chlamydia psittaci has been isolated from the epididymis of young bulls with epididymitis, orchitis and seminal vesiculitis, that is a possible agent producing the clinical seminal vesiculitis syndrome.⁴⁸

***Brucella ovis* (brucellar epididymitis)** is a common venereal disease of sheep causing ram epididymitis and infertility worldwide.^{23,25,27} In California in 1956 examination of 1882 rams revealed a 27 percent incidence of infection. Of 175 ewe lambs bred to clinically normal rams, 75 percent lambed within a 30-day period while only 47 percent of 171 ewe lambs bred to clinically-infected rams lambed during the same period.⁴² In Idaho in 1970, 1890 rams were examined in 37 large commercial flocks. Twenty four percent of the rams were clinically affected and over 97 percent of the flocks were infected. The disease was more common in the black-face breeds and crosses.⁴⁷ Ewes bred to infected rams had a greatly increased number of services per conception and fewer lambs per ewe than ewes bred to non-infected control rams.⁴⁰

The infective organism is spread mainly by venereal contact to susceptible rams breeding a ewe recently bred by an infected ram, or by rams penned together mounting each other and having rectal copulation, penile contact with a contaminated perineal region, or oral infection from infective feed or water.^{1,23,28} Ewes play a minor role in the spread of the infection and are relatively resistant to the infection; but occasional abortions due to ***Brucella ovis*** are reported. Young rams raised from infected ewes are not infected. Rams are readily infected by the conjunctival, oral, rectal or preputial instillation of the organism. Rams may spread the organism for 3 to 4 years while ewes spread infection for a much shorter period of several days after an occasional abortion. Following infection the antibody levels rise by the third to sixth week and persist for up to a year after the end of the bacteremic stage of the disease, which ends in about 60 days. The organisms localize in the epididymis, vesicular glands, ampullae, liver, and kidneys. The organisms cause perivascular lesions with edema and fibrosis in the epididymis resulting in obstruction of the lumen and stasis of the epididymal contents and finally extravasation of semen that, because of its high lipid and mycolic acid content, results in the formation of a spermatic

granuloma resembling tubercular granulomas.^{2,3,34} (See Figure 189.) Over 90 percent of these lesions affect the tail of the epididymis but occasionally the body and head of the epididymis may be involved. If the lesions are unilateral, fertility is normal or only slightly impaired; if they are bilateral, sterility is usually present.^{1,23,50} In 29 naturally-infected rams the semen quality, including motility and concentration was inferior in 50 percent of the rams and normal in only 25 percent.⁴⁰ It takes 1 to 4 months from the onset of infection to the development of the lesions in the tail of the epididymis. The tail, or occasionally other portions, of the epididymis enlarges 3 to 5 times normal size and becomes fibrotic or with an occasional abscess. Some infected rams fail to develop gross palpable lesions.

Diagnosis is based on clinical palpation of the epididymis to detect induration, spermatic granulomas, abscesses and enlargements, especially involving the tail of the epididymis. In advanced cases testicular degeneration, atrophy and later mineralization of the testis may occur. Some affected rams would be difficult to differentiate on clinical examination from those with epididymitis due to other causes such as *C. pseudotuberculosis* or *Actinobacillus seminis*. These latter infections are more sporadic, variable in location and resemble abscesses rather than granulomas. Enlargement of the head of the epididymis is more likely due to granulomas secondary to anomalies of the efferent ducts. The combination of clinical palpation of the testes, culturing the semen and the complement-fixation test on serum was most effective in locating shedders of *Brucella ovis*. Screening tests were run at 1:10 dilutions.² Other serologic tests have included the agar gel diffusion test and the ELISA test.

Controlling ram epididymitis in a flock is highly important to maintaining good fertility in the flock. Before the breeding season all rams that show clinical or serologic evidence of epididymitis should be eliminated. In valuable purebred rams semen examination and culture may be used.⁴⁰ Various vaccination procedures have been used successfully to protect rams against *Brucella ovis*. In New Zealand they have used a combination of *Br. ovis* bacterin and strain 19 *Brucella abortus* vaccine.^{10,46} In the U.S. an alum-precipitated commercial *Br. ovis* bacterin has been developed and approved^{39,41} that is given subcutaneously in two doses 3 to 6 weeks apart and followed by a single injection repeated each year. (Cutter Laboratories and Colorado Serum Co.) This vaccine may occasionally cause a granuloma and some soreness and irritation at the site of the subcutaneous injection behind the elbow, but abscessation is rare. Vaccination causes a serum titer to develop that lasts several years after the combined vaccines were given.⁴⁶ The combination of the

vaccine with other control practices was highly effective in infected flocks of sheep. One study in which clinically affected rams were culled, together with a vaccination program starting with ram lambs 4 to 5 months of age, the incidence of culling dropped from 44 percent at the onset to 2 percent after three years of the trial and remained low for the next 7 years.^{39,41} To rapidly reduce or eliminate the *Br. ovis* infection in a flock, identify and isolate or cull all rams with clinical disease, serologically test and cull positive rams every 30 to 60 days until the incidence is below 1 percent. By testing and isolation practices a *Br. ovis* clean ram flock may be established. A more practical and less expensive procedure is to follow a vaccination program.^{1,23}

Actinobacillus seminis, actinobacillary epididymitis or epididymo-orchitis has recently been described as a venereal disease of rams that is similar in many respects to the foregoing epididymitis due to *Br. ovis*. It also is world-wide in distribution; is transmitted in a similar manner with a similar incubation period and the complement fixation test on serum, clinical palpation of lesions, and culture of semen are used in the diagnosis of the disease. It differs somewhat from the brucellar epididymitis by the frequent development of clinical, unilateral or bilateral orchitis and periorchitis with moderate to severe systemic signs including elevation of body temperature to 40 to 42° C and even death in the early stages of the disease. Subclinical infections are not uncommon. After the acute stage of the disease chronic adhesions around the testes may develop, degeneration, atrophy and even mineralization of the testis may occur. The epididymis becomes enlarged and indurated due to sperm granulomas or abscesses that may involve the head, body or tail or the entire epididymis. Rarely abscesses may rupture through the scrotum and produce a discharging fistula. The diagnosis, prevention and treatment of actinobacillary epididymitis is similar to brucellar epididymitis except no vaccine is presently available for the former disease.^{23,49,50}

Canine brucellosis due to *Brucella canis* is apparently widespread in the U.S. among dogs, especially Beagles,¹² causing abortion in bitches and swelling of the scrotum, firm enlargement of the epididymis, especially in the tail, and degeneration and atrophy of the testis with sterility in males. The disease is spread by direct contact with aborted fetuses, placental tissues and the infective vaginal discharges of bitches for several weeks after abortion. Venereal transmission to females by the semen from chronically-infected males is a common mode of spread. Following exposure a bacteremia develops within one to three weeks with a generalized lymphadenitis. Antibodies develop that can be detected by the agglutin-

ation test; 1:100 is considered positive. These antibodies may last indefinitely or as long as a bacteremia persists. The organisms can often be recovered from the lymph glands, spleen, liver, prostate, testes and epididymides. Clinical lesions need not be present. The prognosis is poor in clinically-affected male dogs. Any possible effective antibiotic therapeutic regimen must be heroic and sustained. If the genital organs are seriously damaged or if the lesions are bilateral, recovery is unlikely. Efforts to develop a bacterin have been unsuccessful. Prevention and control of canine brucellosis presently is based on monthly serologic tests of all dogs in the kennel, and those entering, together with segregation and destruction of positive animals. **Brucella canis** has caused human infections. (See **Brucella canis** abortion.)

The prognosis in severe or moderate epididymitis is poor, as obstructions usually occur preventing the discharge of spermatozoa from that testis. There is no practical cure in animals once the epididymis is obstructed. In the occasional case of bilateral epididymitis the prognosis is hopeless. In recent years operations have been devised to bypass the obstructed portion of the epididymis in humans but the percentage of cures is low.

If in a valuable animal the epididymitis is unilateral and the accessory glands and the vas deferens have no lesions or infection caused by the same organisms, unilateral castration may be indicated followed by a long recovery period for the normal testis during which repeated tests and cultures of the semen may be performed to be certain the genital infection has been eliminated.

Anomalies of the Epididymis may be either congenital or hereditary and consist of: (1) a spermioistasis due to distention of aberrant efferent or epididymal tubules with the secondary formation of spermatic granulomas in the region of the head of the epididymis, (2) segmental aplasia of the mesonephric (Wolffian) duct or ductus deferens and (3) mesonephric or paramesonephric duct cysts or remnants near the epididymis or ductus deferens.^{22,34-36}

Spermioistasis, resulting in spermatoceles and in time, by the same process as described under infections involving the escape of sperm cells into adjacent tissues, spermatic granulomas, resembling tubercular granulomas, may be caused initially by blind-ending rudimentary mesonephric tubules or ductuli aberrantes.^{22,34-36} These tubules most often are defective efferent tubules. They may be attached to the rete or epididymis and therefore produce lesions involving the head region, or caput of the epididymis and only rarely other portions of the epididymis. Spermioistasis was noted in 208 (25 percent) of 836 bulls in one or more of the efferent ducts.³⁶ Sperm granuloma is common in bucks less

common in rams, uncommon in bulls and rare in the other domestic animals. The frequency of occurrence of granulomas is not related to the incidence of blind-ending or aberrant efferent tubules as found in normal animals.^{22,35} In rams it has been confused with ram epididymitis which usually causes spermatic granulomas in the tail of the epididymis. In bucks the condition is usually bilateral resulting in complete sterility. The incidence in bucks in Germany was reported to be 20 to 25 percent and therefore the condition was of great economic importance. In bulls of two Danish breeds the incidence was about 3 percent, and more than 90 percent of the cases were unilateral so most bulls remained fertile.⁴⁻⁷ There was considerable evidence that bovine spermioistasis in the mesonephric ducts is genetically determined by a recessive hereditary factor. The author has observed two related Brown Swiss bulls with spermioistasis and granulomas of the left caput epididymidis. Spermioistasis with spermatocele and spermatic granulomas develop slowly thus young, even bilaterally affected, males may be fertile for a year or more until the fibrous tissue of the granuloma completely obstructs the mesonephric duct. Spermatozoa and fluid are continued to be produced in the seminiferous tubules and absorbed in the efferent ducts and head of the epididymis if the obstruction is located at the distal portion of the head. If the obstruction is located at the proximal portion of the head or in the efferent tubules the pressure may produce testicular degeneration but the size and consistency of the testicle may remain nearly normal due to the accumulation of testicular secretions.³⁴⁻³⁶

Segmental aplasia of the mesonephric or Wolffian duct, epididymis or ductus deferens may occur congenitally in all species but has been well-described in bulls.^{4-7,34-36} The majority of cases are unilateral and the body, tail, entire epididymis, and even a part or all of the vas deferens may be missing. In unilateral cases the bull is fertile. In the latter instance the vesicular gland on the same side may also be hypoplastic or missing. (See Figures 194 and 195.) The incidence of bovine segmental aplasia of the mesonephric duct in Denmark was 0.59 to 1.18 percent.^{4,5} A 5 percent incidence in 828 infertile bulls was recorded in the Netherlands,⁵² while the incidence in 584 "normal" bulls was 1.7 percent. In 12 of 18 Simmental bulls in Switzerland the epididymal aplasia was bilateral.²⁶ This condition has been described in dogs.^{14,29} The author has observed a few cases in Holstein, Guernsey and Angus bulls in New York State. There was a strong indication that segmental aplasia of the mesonephric duct was hereditary as in 19 male offspring of a unilaterally affected bull there were 4 sons similarly affected.⁴⁻⁷ The missing segment was most often lacking

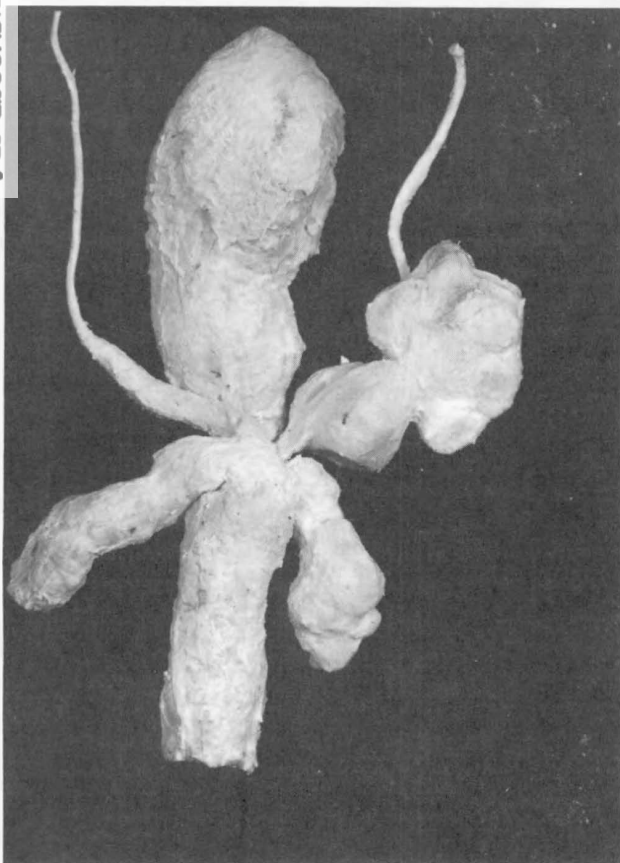


Figure 194. Segmental Aplasia of the Terminal Portion of the Right Ductus Deferens with a Marked Dilation of the Ampulla with Semen in a Bull.

on the right side. In older bulls spermatoceles and/or granulomas may develop just proximal to the missing segment.

In unilaterally affected bulls the sperm cell concentration and the total number of spermatozoa per ejaculate may be about one-half normal. Careful clinical palpation of the testes and epididymides, and a rectal examination of the ampullae and vesicular glands in the larger species will usually detect and delineate the extent of the segmental aplasia. A small epididymis accompanies severe hypoplasia of the testis. The testis associated with segmental aplasia of the epididymis is usually normal in size or may occasionally be atrophied. Palpation of a very small or missing tail of the epididymis is highly indicative of segmental aplasia. The head of the epididymis, if present, is often enlarged due to distention with sperm. If the segmental aplasia is located in the ductus deferens, the tail of the epididymis may be enlarged. In rare cases the missing mesonephric segment may be located in the

ductus deferens near the urethra causing distention of the ampulla. (See Figures 194 and 195.)

There is no treatment for this condition, other than possible surgery to reunite the unaffected portions of the mesonephric duct. Because of the possible hereditary nature of this anomaly affected males should be discarded.



Figure 195. Aplasia of the Right Ampulla and Ductus Deferens and Arrested Development of the Right Vesicular Gland in a Bull.

Mesonephric or Wolffian, or paramesonephric or Mullerian duct cysts or remnants and miscellaneous anomalies may be found in males and are of little consequence except in cases where they may be large and are confused with defects or diseases of the epididymis on palpation. Ectopic rests of adrenal cortical tissue may be found in the testis, epididymis or spermatic cord, especially in the horse.^{34,35} A rare case of a Holstein bull, twin to a freemartin, had an area of testicular rete tissue outside of the testis in the region of the head of the epididymis.¹³ This is commonly observed in the rat. Paradidymides, detached segments of mesonephric tubules, were seen on the spermatic cord and epididymis in 25 to 46 percent of calves and are of no significance.⁵ Occasional mesonephric duct cysts may be found in bulls near the head and tail of the epididymis and some may be lined by ciliated cells, "medusa cysts." Paramesonephric cysts or uterus masculinus are seen commonly in 24 to 44 percent of bulls on the dorsal surface of the urogenital fold between the ampullae and ductus deferens or rarely in or near the epididymis.^{5,6,24}

Primary tumors of the epididymis are rare in all animals. Testicular tumors in dogs or other animals may invade the epididymis or spread through the epididymis to the ductus deferens and cord. Occasionally metastatic tumors such as lymphosarcomas and Sertoli cell tumors in the bull,³⁴⁻³⁶ may develop in the epididymis. Primary tumors of the epididymis are nonexistent in the tom cat and rare in the dog.⁸ Only 2 cases of fibromas of the epididymis in dogs were described.

Miscellaneous Diseases of the Epididymis—Obstruction and enlargement of the epididymis in bulls resulted from a metaplastic process in **hyperkeratosis**.³⁸ Feeding highly chlorinated naphthalenes caused external symptoms of hyperkeratosis and complete sterility. Fertility was gradually regained in about 10 months after withdrawal of the toxic agent. **Sperm granulomas of the ductus deferens and tail of the epididymis secondary to adenomyosis** of the duct wall has been described.³⁴⁻³⁶ This condition may be related to chronic estrogen stimulation. It was observed in 6.2 percent of 695 bulls from an AI center. It has also been observed in dogs with Sertoli cell tumors and in two stallions with secondary sperm granulomas.³⁶ Sperm granulomas may also occur secondary to congenital anomalies, infectious agents, vascular and traumatic lesions and autoimmune reactions. Fifty-three (6.3 percent) of 83 bulls had sperm granulomas of the epididymis.³⁵

There is definite evidence that a **change in the environment of spermatozoa, especially in the tail of the epididymis**, due to probable changes in the epididymal epithelium may result in a reduction or absence of mo-

tility or akinesia or necrospermia associated with bent or looped cells. Testosterone maintains the function of the epididymis. Estrogens injected into adult bulls caused an increase in abnormal bent or looped sperm tails.¹⁶ Frequent collection of these treated bulls resulted in a decline of abnormal sperm cells. Three infertile Jersey bulls with many vacuolated basal epithelial cells of the cauda epididymis and with many secretory granules in the lumen of the duct were reported.¹¹ Inbred Jersey bulls with impaired fertility characterized by poor quality semen with bent, looped and coiled tails, tailless heads, abnormal heads and thickened midpieces were reported later.¹⁷ This genetic condition was caused by a reduced sex steroid production due to the subnormal formation of its precursor, alpha-hydroxyprogesterone.¹⁷

Testicular injury and reduced production of sperm cells, hormonal upsets, as excess estrogen, and insulation of the scrotum produces changes in the epididymal plasma resulting in sperm defects especially reduced motility and tail or midpiece defects. These defects develop in the corpus and tail of the epididymis.¹⁸⁻²¹ Poor sperm cell motility, seen occasionally in stallions, may not be due to an intrinsic defect of the spermatozoa but due to a failure of the epididymis to properly support the cells for their relatively long storage period in that organ.³¹ One of the first and most striking effects following hypophysectomy of young human males was the complete loss of motility in sperm cells already present in the epididymis. Exogenous testosterone therapy was suggested. Three bulls with spermatikinesia associated with a high percentage of bent and coiled tails was described.^{19,21} Exhaustion trials showed that as the storage time in the epididymis decreased the semen quality improved indicating a disturbed function of the epithelium of the cauda epididymis. The sodium and potassium levels in the seminal plasma of the cauda epididymis were very low possibly related to an endocrine imbalance.

Since about 95 percent of pet male dogs are not castrated and therefore contribute to the problem of overpopulation of dogs, it has been reported that a simple operation of injecting 1 ml. of an aqueous solution of 4.5 percent chlorhexidine digluconate into the tail of the canine epididymis, after a sedative dose of "Rompun," produces azoospermia within 4 weeks by causing a sclerosing obstruction of the epididymis or ductus deferens, chemical vasectomy.⁴⁴ Further, such studies should be pursued.

Pathology of the Ductus Deferens and Ampullitis

Infection and inflammation of the ductus deferens is usually associated with an orchitis, epididymitis, or sem-

inal vesiculitis. Infection of the ductus deferens apparently occurs less commonly in animals in which the ampullae or dilated proximal portions of the ductus deferens are absent. In the stallion and bull, infections with organisms such as *Br. abortus*, streptococci, *C. pyogenes*, tubercle bacillus, *Ps. aeruginosa*, mycoplasma, ureaplasma and others including viruses, have been observed. (See infectious causes for orchitis and epididymitis.) The infection is usually unilateral but may be bilateral.

As discussed previously segmental aplasia may occasionally be present in the ductus deferens, usually unilaterally and paramesonephric cysts or a uterus masculinus, are common in the urogenital fold between the two ampullae, especially in bulls.

Careful rectal examination will usually reveal a thickened, firm and possibly painful enlargement when ampullae are diseased. Semen examination may reveal leukocytes and the infective organisms. In some cases the semen contains clots of pus and the motility of the spermatozoa is poor. If the motility is good immediately after ejaculation, the spermatozoa often lose their motility rapidly on storage. In cases of segmental aplasia where the missing segment is near the urethra, the ampullae may become greatly enlarged and distended with spermatozoa but no inflammatory reaction is present. Often the vesicular gland on the same side as the missing segment is also hypoplastic or absent. Treatment of infected or diseased ampullae is similar to treatment for seminal vesiculitis.

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Diseases of the Accessory Glands

Diseases of the Vesicular Gland, (Seminal Vesicle)—Although congenital defects, usually unilateral, of the vesicular glands including hypoplasia, cysts and either absence or doubling of the gland has been reported^{35a,b} often in association with segmental aplasia of the mesonephric duct, seminal vesiculitis is the most common condition found affecting the gland of bulls, stallions and boars. It is rare in bucks and rams. Gross inflammatory lesions are found most commonly in the vesicular gland of the accessory reproductive glands and the ampullae. The incidence of seminal vesiculitis in bulls was reported as 0.8 percent of 2000 bulls examined in Denmark,^{5,6} 4.2 percent of 828 infertile bulls examined in Holland,⁴⁷ 2.5 percent of 7359 bulls examined in Colorado,^{11,12} and 4.6 percent in 343 bulls studied in New York State.^{35a} A bovine seminal vesiculitis syndrome seen in midwestern United States was described⁴ that differed from the usual sporadic cases observed elsewhere. Up to 10 percent, or an average of 5 percent, of groups of young beef bulls running together and fed heavily and grown rapidly for sale were affected. While breeding bulls grown more slowly on limited rations had an incidence of only 1.3 percent. In housing arrangements where 10 to 20 young bulls, 10 to 15 months of age, run together, the incidence of seminal vesiculitis may reach 20 to 30 percent of the bulls.³² These young affected bulls usually recover without treatment. Seminal vesiculitis in stallions and boars is observed less commonly.

Seminal vesiculitis may be caused by a variety of pathogenic organisms. The most common cause in the United States is *C. pyogenes*. (See Figures 196 and 197.) This organism may localize in the seminal vesicle from other primary, pyogenic, infective foci such as rumenitis, liver abscess, traumatic gastritis, lung abscess or from a navel infection in a young calf.^{23,35a,b} It may possibly enter as an ascending or descending infection from the prepuce and urethra or from an ampullitis, epididymitis or orchitis.²⁵ Infection may be spread in groups of young bulls by homosexual activities and contact of the penis and prepuce to the rear parts of a bull that another had recently mounted. It is possible that certain organisms as *C. pyogenes* may invade the seminal vesicle secondary to a temporary infection with a virus or other agent, possibly a mycoplasma.

In countries where brucellosis is still prevalent, *Brucella abortus* is the most common cause for seminal



Figure 196. Seminovesiculitis in a Bull.

vesiculitis. In 30 bulls with positive brucella titers of serum and semen plasma, **Br. abortus** was recovered on culture of guinea pig inoculation of the semen in 15 or 50 percent.⁵ Twenty six of these bulls were examined and had clinical gross lesions in the genital organs and nineteen had lesions found on autopsy. Seminal vesiculitis was found in 17 bulls, ampullitis in 5 bulls, orchitis in 5 bulls, and epididymitis in 2 bulls. In some a combination of lesions were found.

Brucella suis commonly localizes in the seminal vesicles in boars.¹⁷ Examination of 9 boars serologically positive for brucellosis revealed **Brucella suis** in the seminal vesicles of 8 boars, in the epididymides of 6, in the prostate of 4 and in the semen of 7. No macroscopic lesions were present.¹⁶ In 37 boars infected with **Br. suis** orchitis was uncommon, occasional macroscopic lesions were observed in the vesicular glands, while nearly all infected boars had microscopic lesions in the epididymides and vesicular glands so that 75 percent of the boars periodically secreted organisms in their semen.⁴⁵ Pus and leucocytes were seldom found in infected semen. Infertility in boars is frequently associated with the shedding of **Brucella suis** organisms in apparently normal appearing semen. The excretion of **Br. abortus** was reported in the semen of a stallion.⁴⁶ Organisms found in infected vesicular glands included: streptococci and staphylococci in bulls and boars,²² **Pseudomonas aeruginosa** and **Actinobacillus actinoides**,²⁷ *Proteus*,³⁵ *My-*

coplasma bovigentialium^{1,9,20,21,33,37,38,41} and *bovis*,^{30,33} and **Mycobacterium tuberculosis**. **Mycobacterium paratuberculosis** was recovered from the feces and semen from an affected bull used in an AI center.³¹ On necropsy, **M. paratuberculosis** was isolated from the vesicular glands and prostate.

Ureaplasmas have recently been recovered from bovine seminal vesiculitis lesions and reproduced experimentally.^{19,33} **Hemophilus somnus** has been isolated from the accessory sex glands of bulls but not from the testis or epididymis.^{26,33} Although a higher incidence of infection was present in young bulls, the pathological significance of **H. somnus** in the bull awaits further study.

Virus infections described under orchitis and epididymitis have also been reported to cause seminal vesiculitis including the enteric virus, possibly IBR-IPV,¹⁰ and the "epivag" virus.³⁴ **Chlamydia psittaci** was recovered from the semen or organs of 6 to 10 bulls from two beef herds where the seminal vesiculitis syndrome was commonly observed in young beef bulls.^{4,33,43,44} The **Chlamydia** recovered from one of these bulls was indistinguishable from **Chlamydia psittaci** in California responsible for epizootic bovine abortion and enzootic abortion of ewes. The seminal vesiculitis syndrome reported in Colorado^{4,12,44} appeared clinically similar to those described in Wisconsin and Czechoslovakia.^{32,36}

Naturally occurring cases of seminovesiculitis in bulls due to **Mycoplasma bovigentialium** have been described along with experimental studies.^{18,33,38,41} In natural cases the semen was stringy and mixed with pus. The vesicular glands especially the cranial portions were firm, swollen and nodular. Postmortem examination and culture of all portions of the male genital tract showed

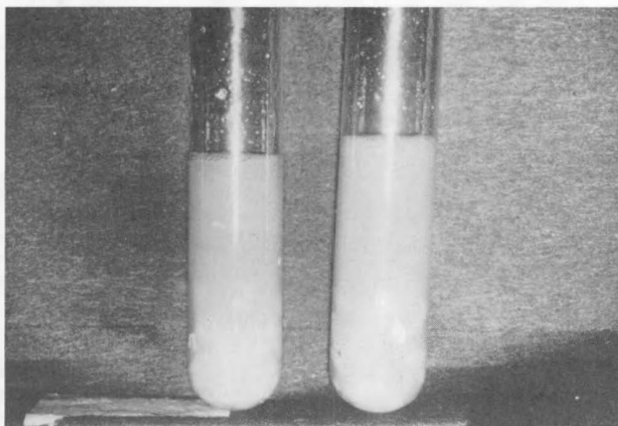


Figure 197. Ejaculates Containing Clots of Pus from a Bull with Seminovesiculitis.

the organism had become widely distributed throughout the tract. The organism persisted in the experimental bulls for at least 17 weeks and could be recovered from the semen for 11 weeks. The usual antibiotics used in extended semen had no effect on **Mycoplasma bovigenitalium**. This organism caused a necrotizing vasculitis in many bulls and was present in the carpal joint of one bull.⁴¹ Earlier studies cited by Parsonson^{40,41} reported the pathologic lesions produced in the genital tract of cows. This could not be confirmed with **M. bovigenitalium**.²¹ However these authors showed the organism was pathogenic for the vesicular glands, udder and joints. Prior to the inoculation of the vesicular glands in the experimental bulls, mycoplasma could be recovered from their preputial and nasal cavities.^{40,41} This could be done also in control bulls but on autopsy no mycoplasma could be recovered from the urethra or internal reproductive organs of the control bulls but could be from the experimental inoculated bulls. After inoculation the viability of the spermatozoa decreased markedly in bulls with seminovesiculitis, ampullitis and epididymitis caused by mycoplasma. Inoculated vesicular glands became enlarged, swollen and nodular. Many polymorphonuclear leucocytes and eosinophiles were present in the inflamed tissues and exudate.

Recent studies have shown that the presence of mycoplasma and possibly ureaplasma, in semen, especially processed frozen semen from normal bulls had an adverse effect on motility often requiring the discarding of that ejaculate of semen. Nine of 14 bulls with a post-thawing motility below 30 percent were positive for **M. bovigenitalium** on culture.²⁴ In a Czechoslovakian study²⁸ 12 of 44 semen samples from which mycoplasma were isolated had low motility, while only 2 of 31 samples free of infection had a low, unsatisfactory motility. This lowered motility might be due to the affinity of the sperm cell for mycoplasma or due to epididymal infection resulting in epididymal plasma alterations that affect the sperm cells.^{38,39} All strains of ureaplasmas (T mycoplasmas) when inoculated into bovine oviductal tissue cultures caused a cilia stopping effect (CSE) progressing to collapse and eventual sloughing of the cilia due to the cytotoxin produced by the organism.^{44a} This effect on cilia may possibly explain the decline in motility of spermatozoa in contact with ureaplasma or mycoplasma since the body and tail of the sperm cell is a modified cilia. It may also explain the infertility in cows when these organisms are introduced into the cervix, uterus and oviducts where cilia perform a necessary function in sperm transport.^{44a} Further studies are needed.

Experimental infection of the vesicular glands with **Mycoplasma bovis** resulted in a persistent infection for

at least 8 months during which time the organism was shed continually not intermittently like **M. bovigenitalium**. Furthermore there was no tendency for the infection to spread to other genital organs as there was with the latter mycoplasma.³⁰ A local semen agglutination response developed that produced higher titers to **M. bovis** in the seminal plasma than in blood serum.¹⁴

Seminal vesiculitis affects males of all ages. In bulls it has been reported as early as 10 months to one and one-half years of age. Usually there are no external signs of the disease. Occasionally however some males will show signs of mild peritonitis with an arched back, reduced appetite, pain on defecation or on rectal examination and hesitation in mounting and thrusting. These occasional signs are observed usually in bulls having abscesses of the vesicular glands caused by **C. pyogenes** infection adjacent to the peritoneum. On rectal examination seminal vesiculitis, especially bovine cases due to the latter infection, are characterized by two general findings, firstly, irregular enlargement of the gland, fibrosis, peritoneal adhesions, loss of lobulations, fluctuation, and abscessation. (See Figures 196 and 197.) In rare cases fistulas occur due to rupture of an abscess into the rectum. In the other more common cases a portion or all of the vesicular gland may become thickened and fibrotic with only slight enlargement and loss of lobulations of the gland and with no adhesions.

The first type of bovine seminovesiculitis was usually unilateral and due to chronic purulent inflammatory lesions with chronic interstitial changes and was commonly caused by **C. pyogenes**.²³ The second type of seminal vesiculitis was usually bilateral and characterized by degenerative changes in the epithelium and inflammatory changes were variable.²³ Cultures of these latter vesicular glands were frequently negative for bacteria. Large amounts of Feulgen positive chromatin masses were found in the lumen of affected glands and in the semen of the latter degenerative type of seminal vesiculitis, but not in the former. In both types varying numbers of polymorphonuclear leucocytes were usually found in the semen. In the former purulent type of seminal vesiculitis large clots or flocculi were commonly observed while in the latter the semen may be viscid or "ropy." Leucocytes in the semen may also come from other portions of the urogenital tract including the prepuce so their presence is not diagnostic of seminal vesiculitis. In some chronic cases few or no leucocytes will be present in the semen of affected bulls. Semen quality will vary between affected bulls, with a lowered motility of the sperm cells, an elevated pH, a high catalase activity, and a lowered fructose content being commonly found. Although lowered fertility has been associated with seminal vesic-

ulitis many affected bulls breeding cows naturally have a good conception rate. One affected bull with good fertility had been used for at least three years in an artificial insemination stud although periodically a number of ejaculates had to be discarded as being unsatisfactory.^{35a} In thirty cows bred to an affected bull, 7 or 23 percent aborted from three months to term.^{35a} In bulls with seminal vesiculitis 40.5 percent had satisfactory quality semen and 50 percent had semen of questionable quality, while normal bulls had 83.7 satisfactory and 11.7 percent questionable quality of semen.

The use of a bull for artificial insemination with *Brucella abortus* infection of the accessory glands or ampullae may spread the disease and cause infertility. One infected bull used artificially infected 71 percent of the cows in 41 *Brucella*-free herds.⁴² In young beef bulls with the seminal vesiculitis syndrome, 8 of 10 affected bulls had substandard quality of semen and leucocytes were consistently found in the ejaculate.^{11,12}

Blom^{5b} reported on 25 bulls with seminal vesiculitis and/or ampullitis of which 10 had malformations of the excretory ducts including: segmental aplasia or hypoplasia of the Wolffian duct, accessory vesicular glands, persistent uterus masculinus and asymmetrical implantation of the ampullae. These anomalies possibly interfered with closing of the duct orifices in the colliculus seminalis predisposing to bacterial infection. The possible genetic transmission of these defects together with the poor prognosis of a cure favors slaughter of the animals.

Not infrequently bulls with a seminal vesiculitis will have another focus of infection in the testis, epididymis or ampulla. In the seminal vesiculitis syndrome, especially in groups of young beef bulls, focal or diffuse nonsuppurative interstitial inflammatory lesions were commonly present in the epididymides, testes, ampullae, prostate and less commonly in the bulbourethral glands.⁴ This widespread infection of the male reproductive tract was also found in mycoplasmosis due to *M. bovis genitalium*.^{1,2,18,33,38,41} The viruses and Chlamydia recovered from diseased vesicular glands by African³⁴ Czechoslovakian³⁶ Belgian¹⁰ and Colorado⁴⁴ workers also affected a number of the reproductive organs besides the vesicular glands. In the seminal vesiculitis syndrome, however, the principal signs are related to the vesicular glands.⁴

Diagnosis is based on the clinical signs noted above. Ampullitis and prostatitis may be difficult to diagnose by rectal palpation in the bull and stallion. Culture of the semen is usually an unsatisfactory method for diagnosing the causative bacterial agent because of the contamination from the sheath. A technique was developed to collect non-contaminated urethral samples from

bulls.⁴² A tranquilizer was administered to quiet the bull and allow withdrawal of the penis. Rectal massage aided the protrusion of the penis from the sheath. The penis was washed with an antiseptic solution and the urethra was irrigated with sterile saline. A 10 inch or 25 cm. sterile silastic tube was inserted up the urethra leaving 1 or 2 inches, about 4 cm. protruding. Rectal massage of the vesicular glands, prostate and ampullae resulted in the collection of their secretion into sterile vials for cultural purposes.⁴² Only 4 of 158 urethral samples were contaminated.

The prognosis in seminal vesiculitis is fair to poor depending upon the causative agent, the presence of other foci of infection in the reproductive tract, the duration and severity of the infection and the value of the male. Males with *Brucella* infections, tuberculosis or possibly mycoplasmosis of the seminal vesicles, or those with secondary lesions of the testes, epididymides, ampullae or prostate should be slaughtered. Many young bulls with the seminal vesiculitis syndrome with catarrhal or degenerative seminal vesiculitis overcome the infection spontaneously in a few months.^{12,32} During this period their use for breeding purposes is questionable. Bulls with active acute lesions of seminal vesiculitis with a discharge of pus in the semen should not be used for artificial insemination as only rarely will the antibiotics used in extended semen destroy the organisms present. Many bulls with seminal vesiculitis caused by organisms other than *Brucella* or *Mycobacterium* may be used naturally or even artificially with quite satisfactory conception rates especially if a large amount of mucopurulent material is not present in the ejaculate. Further studies on the possible viral causes of this disease and the duration of the carrier state is definitely needed.

Treatment with high levels of broad range antibiotics, or antibiotics to which the causative agent is sensitive, for two weeks or longer together with mild massage of the vesicular gland to remove its contents may result in recovery or elimination of the infection in some males after 2 to 6 months. In *C. pyogenes* infection the gland is usually left severely indurated and largely destroyed. Acute cases of seminal vesiculitis tend to become chronic. Chronic cases, if abscessation does not occur, tend to become fibrotic and indurated similar to the mammary gland following a severe infection. In long-standing chronic cases pus or high leucocyte numbers are seldom observed in the semen.

In recent years surgical removal of the affected vesicular glands has been recommended for selected bulls in artificial insemination studs or where conservative treatment has failed or is not deemed advisable, and where the only detectable lesion of the genital tract is in the

seminal vesicle and extensive adhesions are not present. In an aseptic manner and under epidural and local anesthesia together with tranquilization, an elliptical incision was made in the ischiorectal fossa after suturing the anus tightly closed.^{15,29,35a} By a combination of blunt and sharp dissection the affected gland was isolated and removed close to the urethra after ligation at that point. Some difficulty was experienced if adhesions were present especially in separating the peritoneum from the cranial portion of the gland. Following surgery heavy prolonged antibiotic therapy was recommended. The results were satisfactory in all cases except in one bull that developed a degree of paralysis in the sphincter of the bladder with cystitis and urinary complications.

Regular and frequent examination of the genital tract and semen for a year or more should be followed after treatment to be certain the condition doesn't recur at another site due to a resistant or secondary focus of infection.

Disease of the prostate gland is rare in all animals except the dog in which acute or chronic prostatitis and benign prostatic hyperplasia (BPH) are common. Other less common canine prostatic diseases include neoplasms, retention or congenital cysts and rare calculi.^{7b,8} The disease conditions affect all breeds of dogs equally. These diseases in the dog resemble those in man.¹⁶ About 60 percent of all intact male dogs over 5 years of age have enlarged prostates usually due to BPH. Infection in the prostate gland may be a source of bacteria for recurrent cystitis.^{7b,8,11,12} A combination of the above prostatic lesions is not uncommon in old dogs. On rectal palpation of the prostate, abscesses, retention cysts, and tumors are characterized by asymmetrical enlargement of the gland. The other pathological conditions are usually symmetrical.^{11,12} Almost all prostatic diseases are usually clinically characterized by either or all lower urinary tract signs, systemic signs, especially in acute prostatitis, and abnormalities or difficulties in defecation.^{8,11,12}

Prostatitis in the dog is often associated with hyperplasia of the gland. It is probably due to an ascending infection through the urethra but may occur secondary to hematogenous infection or even descending infections. A wide variety of organisms have been isolated from infected glands including *Brucella canis*, *E. coli*, streptococci, staphylococci, *Proteus* and rarely blastomycetes.²² Acute prostatitis in the dog is a diffuse or local suppurative inflammatory reaction with a tendency for abscess formation.¹⁹ Bacteria, leukocytes, and blood are frequently found in the urine, the latter portion of the ejaculate, or observed at the preputial orifice. This should be differentiated from a balanoposthitis. Acute prostatitis

may be painful and characterized by constipation, in arched back, tenesmus, dysuria, elevated temperature and pulse rate, occasionally anorexia and vomiting, and a leucocytosis. Palpation of the infected gland per rectum causes pain and "splinting" of the abdomen. Chronic prostatitis is occasionally observed and may be associated with benign prostatic hyperplasia.^{6,7b,8,11,13a,b,14,19}

The treatment of prostatitis is frequently successful. Administration of broad range antibiotics are indicated over a prolonged period. If the ordinary antibiotics do not control the infection, cultures of the prostatic secretions may be made and the antibiotic sensitivity of the causative organism determined. Laxatives and supportive therapy may be indicated. If prostatitis is due to *Brucella canis* the prognosis is poor. (See *Brucella canis* abortion.)

Clinical prostatitis in the bull and boar is rare and may be caused by *Brucella abortus* or *suis*. Subclinical infections may be more common and due to a variety of bacteria and viruses as described under seminal vesiculitis.

Benign prostatic hyperplasia (BPH) is present in about 50 percent of dogs over 5 years of age that have not been castrated.^{7b,8} The condition is probably due to an endocrine imbalance with an excess of testosterone being secreted which causes an enlargement and hyperplasia of the gland. Some speak of this condition as prostatic hypertrophy but this terminology is not correct. The moderate to greatly enlarged gland may be smooth or nodular and may contain small cysts. When cysts are not present the preputial discharge from an infected hyperplastic prostate is usually purulent; when cysts are present the discharge is watery-grey or bloody. This cystic fluid may be voided with the urine producing albuminuria. Usually dogs with marked prostatic hyperplasia are constipated. Rectal impaction and tenesmus and stranguria predispose to rectal dilation and the development of a perineal hernia. Occasionally cystitis and hydronephrosis may develop. Usually little discomfort is shown by the dog with a hyperplastic prostate unless constipation, stranguria, or perineal hernia occurs.^{1,7b,8,11,12} Severe obstruction of the urethra does not occur in dogs as in man because of the bilobed-nature of the gland in the dog in contrast to the trilobed structure of the gland in man. Rarely the bladder may become strangulated in a perineal hernia.

Digital examination of the prostate bimanually per rectum and by abdominal palpation may reveal a nodular or smooth, enlarged prostate. It is often helpful to exert pressure through the abdominal wall at the pelvic brim to push the prostate caudally so that it can be palpated rectally. The consistency will vary with the nature of the hyperplasia from firm and fibrous, to soft, or even fluc-

tuating if cysts are present. Normal prostate glands are 2.5 to 3 cm. in diameter while hyperplastic glands may be twice as large or even larger if cysts are present. Prostatic cysts often occur with benign prostatic hypertrophy or from blocked prostatic ducts or vestiges of the Mullerian duct. No signs are observed until these cysts become large and press on the bladder or rectum with resulting dysuria or tenesmus with constipation.^{7b,8} Large cysts and abscesses frequently extend into the abdominal cavity. The latter are fatal if they rupture or leak intraperitoneally. A prostatic cyst in a Great Dane dog contained 15 quarts of a sanguineous fluid.¹⁴

A number of diagnostic procedures have been used to determine the nature, severity and type of prostatic disease including palpation, per rectum, ejaculation,^{7b} prostatic massage, aspiration and punch biopsy, radiography and contrast radiography, culture of urine or prostatic secretions, and in acute prostatitis white blood cell counts. These tests must be carefully performed, interpreted and evaluated with skill and experience together with a complete history and physical examination,^{2,4,7b,8,11,12,17} before treatment is recommended, particularly in older dogs and in recurrent prostatic problems.

Rectal massage of the gland may give temporary relief by reducing the size of the cysts. Estrogenic therapy with oral or injectable estrogens in low doses have been used in prostatic hyperplasia. Antibiotics should be administered along with estrogenic therapy. During estrogenic therapy it is desirable to monitor the blood picture to diagnose incipient myelotoxicosis. Gradually reducing the dose during the next few weeks may give relief but continued dosing is required. Estrogens act by suppressing the pituitary gonadotropins and this causes an atrophy of the Leydig cells and suppression of testosterone production. The estrogens do not directly antagonize the androgens. The most satisfactory method of reducing the size of the prostate is castration, as this removes the source of the androgen causing the hyperplasia. Within 2 to 3 weeks after castration the prostate gland begins to noticeably involute and by 6 to 8 weeks it is relatively small in size and atrophied. However castration does not reduce the large cysts or abscesses in infected glands or affect calculi that may rarely be present.^{8,18} In complicated cases, prostatectomy or marsupialization of the large cyst or abscess through the abdominal wall may be indicated.^{1,3,8,11,12} The urethra is transected and anastomosed into the neck of the bladder and the ducti deferentia are ligated and the proximal portions are removed. When perineal hernias have developed, perineal herniorrhaphy may be indicated.^{15,23}

Squamous metaplasia—The effect of prolonged estrogen stimulation of the prostate gland has been de-

scribed.^{8,10,11,12,19} In dogs with Sertoli cell tumors of the testes, estrogens produced by the tumor cause squamous metaplasia with enlarged cystic prostate glands or atrophy of the glands. These lesions can be produced experimentally by administering estrogens and this is another reason why castration is a more effective therapy than estrogen administration. Furthermore high prolonged dosing with estrogens may cause anemia, leucopenia and aplasia of the bone marrow.⁶ Estrogen-induced changes in the prostate are apparently irreversible in the dog. A squamous metaplasia of the uterus masculinus may also occur.

Similar, but reversible, prostatic lesions to those in the dog, occurred in wethers grazing on certain clovers such as red clover or subterranean clover that contained high levels of estrogens.⁵ The bulbourethral glands also became cystic, dilated with urine and debris and greatly enlarged in castrated sheep. In some cases urinary obstruction, prolapse of the rectum and even death occurred. A similar condition occurred in wethers in feed lots if their ration was supplemented with excessive estrogens or estrogen implants were given to provide growth stimulation.⁹

Adenocarcinoma of the prostate in the dog is rare. It is usually seen in dogs over 10 years of age.^{6,8,10,11,12,16,19} Only 3 cases of carcinoma in over 500 diseased prostate glands were reported.²¹ Persistent straining at the time of defecation was characteristic of all 3 advanced cases. Pain was a commonly observed symptom. Adenocarcinoma of the prostate results in a nodular asymmetrical enlargement of the gland. The tumor may vary in consistency from very hard to soft and is slow to metastasize and therefore signs of disease are seldom observed until the condition is terminal with emaciation and locomotor difficulties.^{8,11,12} A biopsy may reveal the nature of the tumor and differentiate it from benign prostatic hypertrophy (BPH) in the early stages.^{4,17} Castration, estrogen therapy and radiation therapy are of definite value in man in delaying the growth of the tumor even though metastasis has occurred.¹³ Prostatectomy would be indicated if the carcinoma had not metastasized. However the prognosis is poor. Other tumors of the prostate are very rare; these include: leiomyomas, fibromas, sarcomas and hemangiomas.^{10,11} Two cases of adenocarcinoma of the prostate in the tom cat were reported.¹¹

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Diseases of the Accessory Male Glands

A. Diseases of the Seminal Vesicles

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Miscellaneous conditions in the male animal including infection of the external genitalia. Tumors of the penis and prepuce have been described previously in this Chapter.

Perianal (circumanal) gland neoplasms are seen only in dogs and usually around the anal ring and tailhead but also may be found elsewhere on the body. The neoplasms involved are adenomas which are androgen dependent and carcinomas which are not androgen dependent and which must be differentiated from squamous cell carcinomas and adenocarcinomas arising from the anal sac or skin.^{4,29} Of 472 dogs with perianal gland neoplasms about 82 percent were adenomas and 18 percent were carcinomas. About 80 percent occurred in male dogs, 10 to 15 percent in spayed females and about 5 percent in intact females.^{4,29} Dogs of the Cocker Spaniel, English bulldogs, Samoyed and Beagle breeds were most often affected.

The preferred treatment of perianal gland adenomas is castration rather than excision. In ulcerated or recurrent cases excision should be considered. In 123 dogs with adenomas only 7 had a recurrence of the adenoma after castration.²⁹ About 10 to 20 percent of the perianal gland neoplasms (PGN) and nearly all of the carcinomas were malignant. Many metastasized to the iliac lymph nodes as determined by rectal palpation with resulting constipation and tenesmus. Most of these cases are inoperable and do not respond to castration. Radiation or chemo-

therapy has been tried in these cases with limited success.²⁹

Infections of the prepuce, penis, terminal urethra and semen with bacteria, molds, protozoa, viruses and fungi occur in all male animals from the external environment and from infectious diseases of the upper urogenital tracts. In normal healthy animals the upper urogenital system is free of infectious organisms. However because of the location and structure of the prepuce and free portion of the penis, similar to the vestibule and caudal vagina in the female animal, these organs harbor a wide variety of saprophytic and occasionally pathogenic organisms usually without any clinical signs of infection (See diseases of the prepuce and penis). Certain organisms present in the prepuce of "carrier" animals are considered to be venereal in nature and transmitted from the male to the female and cause an infectious disease of the reproductive tract. The organisms that are transmitted from the male prepuce to the female vagina at coitus are usually considered to be contaminants if no infectious inflammatory process is produced. A local infectious inflammatory process is most apt to occur if an older male is bred to a virgin female. A vulvitis, vestibulitis or vaginitis may develop with a secondary reaction of lymphoid tissues resulting in granular venereal vulvitis or vaginitis in the cow, ewe or bitch. This is followed in time by a local immunity with a regression of the inflammatory reaction. If organisms from the prepuce and penis are carried into the uterus at coitus as in the mare, bitch and sow, temporary or prolonged endometritis may result depending on the degree of resistance or susceptibility of the female animal and the time required for immunity to develop.

In artificial insemination in animals even if the collection and storage of semen is performed in a manner approaching asepsis many organisms from the penis and prepuce are in the ejaculate. In one study in stallions the mean bacterial population in undiluted semen collected in the above careful manner was 573,000 organisms per ml. Twenty one different species of bacteria were isolated many of which were potentially pathogenic.²⁵ Culturing the penis and preputial cavity is of questionable value in the diagnosis of infertility because of the large number and variety of organisms recovered. However, it is of value in specific venereal infections to detect a carrier animal and after treatment to determine if he is free of the infection.⁵ (See culturing of the stallion in CEM and the bull for vibriosis and trichomoniasis.) Schultz and co-workers have described a practical method to test bovine semen samples for specific pathogen-free bovine semen.^{21,22}

A compilation of the infectious organisms recovered from the prepuce, penis and semen of animals follows:

Organisms resulting in venereal infections and diseases:

in cows— *Brucella abortus*, *Campylobacter fetus venerealis* (vibriosis), *Trichomonas fetus*, *Mycoplasma bovis genitalium*⁶ **IBR-IPV virus**, **epi-vag virus** in Africa, ureaplasmas,⁶ rarely *Mycobacterium tuberculosis*, **Paratuberculosis**^{16,26,27,28} and possibly papilloma virus²¹ and Chlamydia.²⁴

in mares— *Hemophilus equigenitalis*, *Trypanosoma equiperdum* (Dourine), and equine herpes virus 3 (equine coital exanthema) [Possible "venereal" diseases, depending on the virulence and numbers of organisms introduced and the susceptibility of the mare might also include: *Pseudomonas aeruginosa*^{10,12} *Klebsiella pneumoniae* var *genitalium*, *Streptococcus genitalium* and *Actinibacillus equuli* (Shigella)]

in ewes— *Brucella ovis* and *melitensis*, *Actinobacillus seminis*, and *Spherophorus* (*Bacillus*) *necrophorus* (lip and leg ulceration) and *Toxoplasma gondii*⁷

in sows— *Brucella suis* and possibly *Staphylococcus aureus*

in dogs— *Brucella canis*⁹ and the transmissible venereal tumor

Other organisms, often called "opportunists" found in the prepuce that may either contaminate or infect females at coitus or by artificial insemination are numerous and varied and include: the ubiquitous Gram negative and Gram positive organisms and fungi and yeasts^{15,21} the most common of which are:

Streptococci spp, *Staphylococci* spp., *E. coli*, *Corynebacterium pyogenes*, *C. renale*, *Alkaligenes*, *Enterobacter* spp., *Serratia*, *Bordetella*, *Citrobacter* spp., *Proteus* spp., *Bacillus* spp., *Micrococcus* spp., *Spirochetes*, *Leptospira* spp., *Actinobacilli*, *Actinomyces* spp., *Aspergillus*, *Absidia*, *Rhizopus*, *Madura*, *Candida* (*Monilia*)^{15,20} and others.

Viruses other than those causing venereal diseases may be transmitted by bovine semen including foot and mouth disease,^{3,13,21} bovine virus diarrhea-mucosal virus (BVD-MD),^{13,23} blue tongue^{8,13,21,22} ephemeral fever, bovine enteroviruses, parapoxvirus, lumpy skin disease virus, and others.¹³ Schultz stated that it is reasonable to assume

that bovine adenoviruses, corona viruses, enteroviruses, parvoviruses and rotaviruses which are ubiquitous contaminants are occasionally present in semen but there is no evidence they play a role in genital disease or infertility.²¹ Swine semen can contain foot and mouth disease virus, swine vesicular disease virus, parvovirus, picornaviruses, adenoviruses and Japanese encephalitis virus.^{13,18} Semen should be obtained from bulls in studs free of the virus as determined by repeated serologic tests or semen cultures.^{13,21,22} Maintaining a high level of immunity by repeated vaccination with an efficacious inactivated BVD virus vaccine or with an attenuated nasal vaccine for IBR-IPV will probably prevent the elimination of these common viruses in the semen of bulls.^{22,23}

In one study a positive relationship was made between bulls latently infected with blue tongue virus that could be recovered from their semen and the presence of vesiculations between the acrosome and nucleus and virus-like particles in the affected spermatozoa.⁸ These vesiculations were different from the vacuoles, "craters" or "pouches" in the nuclear envelope of spermatozoa described previously in which the defects were hypothesized to be caused by a virus. (See spermatozoan abnormalities.)

Currently there is no definite evidence that viruses such as parainfluenza 3 virus¹³ bovine leukemia virus^{1,13,14,22,28a} or porcine pseudorabies virus¹⁷ are spread in the semen. Bovine herpes mammillitis virus has not been reported to have been found in semen.²² *Hemophilus somnus* apparently is part of the resident bovine preputial flora.¹¹ It should be noted that a number of these organisms are also common contaminants or residents of the upper respiratory tract.

It is impossible to eliminate all organisms from the prepuce and free portion of the penis or the caudal portions of the female genital tract. However it is definitely desirable to control the venereal diseases and to prevent heavy contamination of the anterior or deeper portions of the female genital tract with virulent organisms especially in susceptible females with low resistance. The control and prevention of the venereal diseases have been discussed under the chapters on infertility in the various female domestic animals.

To control the severe contamination of the female genital tract with organisms from the males' prepuce at coitus various breeding hygiene practices have been followed with bulls¹⁵ and horses. The mares' external genitalia and perineal region are carefully washed with soap and water and rinsed thoroughly. The tail is banded and the mare is restrained. The stallion's genitalia are also washed with a bland soap and water and thoroughly rinsed before copulation. Excessive dust, sawdust, sand or mud in the breeding shed or area is to be

avoided. As mentioned under infertility in mares excess washing and the use of antiseptics on the stallion may irritate the prepuce and penis, may severely alter the "normal" bacterial flora and/or favor the development of strains of bacteria resistant to the antiseptic (chlorhexidine) and possibly other antibiotics.^{2,12,19a} In the boar surgical removal of the preputial diverticulum may reduce preputial bacteria. The author has attempted to "douche" bulls' sheaths prior to collection of semen in a sterile artificial vagina with very limited success in reducing bacterial contamination of semen.

If artificial insemination is practiced the extension of the semen with extenders containing antibiotics has been a common and successful practice in reducing the numbers of bacteria introduced into the genital tract of the female and has resulted in an improvement in conception rates (See vibriosis or campylobacteriosis in cattle). The use of lincomycin and spectinomycin semen extenders to control mycoplasmas and the further addition of minocycline HCL to also control ureaplasma has been reported.⁶ The use of an extender containing penicillin and gentamycin greatly reduced the bacteria in the semen and prolonged the viability of the equine spermatozoa.^{25a} In a study comparing polymyxin B sulfate and gentamycin it was recommended that the preferred antibiotic treatment for equine semen to control *Klebsiella* and *Pseudomonas* organisms was 1000 units of the former antibiotic per ml. of extended semen.^{25b} The semen should be added to the fresh skimmed milk (heated to 95° C for 4 minutes in a double boiler before its use) extender with antibiotics and incubated at 38° C for at least 15 minutes to permit the bacteriocidal effects to occur. Similar results have been obtained with bull and boar semen (See artificial insemination). To help prevent carrying the ubiquitous ureaplasmas, mycoplasmas and other organisms from the vulva and caudal vagina into the cervix and uterus on the insemination pipette, a sterile plastic cannula, through which the pipette may be inserted, can be used.⁶ Further studies on this practice should be conducted as a recent report indicated that routine use of a "protected" or "double" sheath was of questionable value.^{19b}

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DIAGNOSIS OF STERILITY AND INFERTILITY IN THE MALE AND EVALUATION OF BREEDING SOUNDNESS

The examination of a male animal to assess his fertility or breeding soundness includes both objective and subjective tests or observations usually during a single examination or over a short time period. This results in a value judgment or opinion on the part of the veterinarian. Its scientific validity is limited by the number and frequency of tests performed, their objectivity and their repeatability. In referred laboratory tests the expertise of the laboratory personnel in the fields of serology, microbiology, and pathology are also involved. Most males can be categorized as either a satisfactory potential breeder, a questionable potential breeder or an unsatisfactory potential breeder.⁹ However, a single breeding soundness examination does not indicate the males' past soundness nor his ability to cause conception in the future since too many unknown variables of management, nutrition, and disease in the male and the females to which he was, or will be, bred make retrospective or prognosticative specific judgments uncertain. For this reason the veterinarians' knowledge and experience in the fields of male anatomy, physiology, behavior and pathology are

of paramount importance in arriving at a considered judgement or opinion. The client should be informed that this is an opinion and not an absolute factual determination unless the findings conclusively indicate the male is permanently sterile. As the late noted Nils Lagerlof stated to the author, "Never indicate that a certain male is fertile based on your examination; only indicate that you see no reason why this male should not be fertile."

Since much more basic and applied research over the past 30 years has been conducted on bulls than other male animals, the discussion in this chapter on male infertility will emphasize the bovine species. However, the similarities between males of all domestic species are so marked all species are included.

The breeding soundness or fertility examination of male animals is usually requested in three situations; a pre-purchase or sale examination for either the buyer or the seller or both; the prebreeding season examination in beef bulls, stallions or rams to assure fertile males are used during the breeding season; and when an infertility problem arises in the females bred to the male to determine if the male was the cause of the problem and if so whether the condition in the male is temporary or permanent. Thus the primary objective of evaluation of breeding soundness is to determine which males are infertile so they may be temporarily or permanently eliminated from breeding. ^{1,2,6a,11} (Bulls)10, 19 (Stallions)6, 12 (Rams&Bucks)7, 8 (Boars)8b (Dogs&Toms)6a,8

Historically breeding soundness evaluations (BSE) in bulls was developed in Colorado by Drs. H. J. Hill, L. C. Faulkner, J. S. Scott, J. A. Scott, E. J. Carroll and L. Ball, following severe winters in the late 40s' and 50s' when frostbite of the scrotum of range beef bulls resulted in severe herd infertility in subsequent breeding seasons. These evaluations were made possible by the development of the bovine electroejaculator to obtain semen samples. The results of a study from 1954 to 1962 of 10,940 beef bulls in Colorado revealed that 79.2 percent of the bulls were satisfactory potential breeders, 11.2 percent were questionable potential breeders and 9.5 percent were unsatisfactory bulls to be culled or withheld from breeding.¹ A similar study of 1,005 bulls in Missouri produced similar results of 83.5, 9.8 and 6.9 percent, respectively.² Less than 0.5 percent of bulls in both studies were unable to be classified. A similar report on 1,846 bulls examined over a period of 19 years for use in artificial insemination has also been published.⁶ Both mature and immature bulls were examined and 17 to 19 percent of the bulls were rejected as unsatisfactory.

The examination for infertility of any sire should be careful and thorough, following a definite procedure so that no symptom or lesion will be missed. A complete

record of this examination should be made as the examination progresses. A careful, complete examination of a male is essential to the assessment of his breeding potential. This examination of the male should consist of three major components (1) history and/or breeding records, (2) physical examination including the assessment of libido or sex drive and the various serological, cultural and other diagnostic tests and (3) the examination of the semen.

History and Records—Breeding records are very helpful in the diagnosis of fertility. If the male was bred to a sufficient number of normal females, these records accurately indicate the relative fertility of the sire. If possible these records should be reviewed for two time intervals of 1 to 2 years and the past 6 months. This review will indicate the number of services per conception over a period of several years as well as the past few months, which is of value in diagnosing whether a venereal disease or a pathologic condition affecting the sire is acute or chronic. If records are not available, pregnancy examinations on females recently bred by the male may be necessary. The records of the females bred to this male should be reviewed to see if there is an increased incidence of abnormal genital discharges, delayed estrus or abortions occurring after breeding, indicating possible vibriosis, trichomoniasis, canine brucellosis or the presence of some other disease causing the early or late death of the embryo or fetus. If two or more males are used for natural breeding in the same herd the breeding records may be necessary to determine if one or more bulls are infertile. The conception rate in a pasture-bred herd may be a good index to the fertility of the bulls in that herd.

If possible a number of the daughters of the bull examined should be observed for conformation and the presence of any inherited defects; also, their conception rates should be noted. In multipara the litter size, and viability of the offspring of the sire and his daughters should be noted. The breeding records of the male's sire and dam should be reviewed if they are available. These animals and/or their relatives should be examined or a record obtained for any evidence of hereditary disease. If the male's sire and dam are dead the reasons for their death should be checked. Bulls that have been operated upon for umbilical hernia, deviated penis, or other defects are not desirable, as they may transmit these defects.

The health history of the male should be reviewed. Any illnesses, especially those requiring veterinary treatment, should be investigated. This review should include diseases suffered as a young animal as well as any recent sickness. The records of any and all preventive

vaccinations of the male should be secured. Information should be obtained on the ration fed the male, the amount and frequency of feeding and whether any signs of nutritional deficiency are present.

The physical examination of the male consists of noting the following: his age, according to his registration papers and his teeth; his conformation and the condition of his hoofs, limbs, and joints; any defects either congenital, hereditary, or acquired, and their severity; his general condition, attitude, temperament and hair coat. Obesity and emaciation are serious concerns in breeding males. The body temperature should be taken and a careful clinical examination made of the eyes, circulatory, respiratory, digestive, urinary and lymphatic systems, for evidence of disease that might affect his present or future health. Any unusual symptoms such as coughing, nasal discharge, bloody urine, persistent or intermittent diarrhea, and icterus should be carefully investigated. The teeth, oral cavity, eyes, and face should be examined for actinomycosis, carcinoma, blindness, or other lesions. A rectal examination of the kidney(s) and bladder, accessory sex glands and ductus deferens (ampullae) iliac lymph glands, and internal inguinal rings should be performed in large animals.

If the conformation of the male is poor or defective, the gait and manner and ease of mounting should be observed carefully. Too straight or "postleg" rear limbs, arthritis and spastic syndrome in bulls are frequently associated. Slightly "sickle-hocked" bulls and bulls with a good heel are preferred over the former. It is also desirable to discriminate against males with other conformational defects including: sickle-hocks, bow-legged or camped behind rear limbs.⁹ Any signs of posterior weakness or paresis as indicated by a limp flaccid tail and ataxia is very undesirable in breeding males. If rear limb lameness is present the joints should be examined for arthritis and the hooves examined for pododermatitis, deformities, laminitis or quittors. Twenty five percent of 600 boars purchased over a two-year period by 71 producers in Illinois were never used due to lameness or lack of libido.¹²

The examination of the male in the presence of the female is desirable and necessary in order to observe the degree of sexual desire or libido, which may vary from no interest in the female to extremely eager mounting. Any abnormalities, hesitancy, or evidence of pain on erection, mounting, copulating, and ejaculating should be noted. Tests for libido or sexual desire are often difficult, time consuming and hard to adequately carry out on a large number of males. (See prior discussion in this Chapter.) However in a cited study⁹ 20.6 percent of 548 bulls were culled as poor potential breeders with 55 per-

cent of those culled for physical abnormalities, 43 percent for poor libido or serving capacity and only 2 percent for poor semen quality. At this time the penis and prepuce should be examined for evidence of inflammation, granular venereal disease in bulls, tumors, adhesions, congenital short penis, phimosis, and deviation of the penis. Any history or evidence of vices or bad habits should be watched for before and during the physical examination. In some males it may be desirable to examine the penis further, if necessary under tranquilization, a pudendal nerve block, or general anesthesia. Some owners who sell purebred males take a motion picture of the male copulating with a female before a sale, to prevent having the male returned with the report that it would not copulate normally. At this time the male's gait and manner of moving, his positioning of himself on the mount, his seeking actions with his penis, his intromission and thrusting action and his dismounting are also noted. Any lameness or abnormal gait should be closely investigated. Spastic syndrome, or "stretches," in bulls may not be noted in the early or mild cases unless the bull is seen as it rises or is backed. Promptness and vigor of intromission and ejaculation, however, are not a guarantee of fertility.

The rest of the reproductive system should be carefully examined, clinically.^{9,11} (See Stallion,⁶ ram and buck,^{7,8} dog^{6a} and boar.⁸) The testes, epididymides, spermatic cord and scrotum may be examined by palpation. This should be done bimanually with the large male properly restrained or tranquilized to prevent injury to the examiner. The size and shape of the scrotum and the position of the testes in the scrotum should be observed. Any wryness or difference in the appearance of the two sides of the scrotum should be a cause for further careful examination. A "tilted" or "horizontal" testis in a bull is often located dorsally in the scrotum due to a misplaced attachment of the cremaster muscle resulting in testicular degeneration and atrophy. The testes should be palpated for size, shape, consistency, and the presence of adhesions to the scrotum. The scrotum of bulls, rams and possibly stallions should be measured by tape, calipers or ones' fingers. Any unusual findings should be compared with the other testis or with the testes of a normal male if one is available. The head, body and tail of each epididymis should be carefully palpated for enlargements, missing segments, granulomas and abscesses. Any unusual softness, firmness, swelling, atrophy, heat or pain in the testes, scrotum, or epididymis should be carefully checked. This examination will reveal the possible presence of scrotal hernias, cryptorchidism, testicular hypoplasia, segmental aplasia of the mesonephric duct, varicocele, hydrocele, adhesions, tes-

testicular degeneration, fibrosis and mineralization (calcium deposition), testicular atrophy, orchitis, possible tumors, and other testicular, epididymal, or scrotal pathology.

Semen production is closely related to testicular size and consistency. Many workers^{11,17,18,29} have reported a close relationship between scrotal circumference, and the number of spermatozoa produced in exhaustion trials in bulls. There was no relationship between the scrotal size and body size on the numbers of sperm cells in a single ejaculate. The average scrotal circumference in bulls is as follows:

A Compilation of Measurements of Scrotal Circumference in Centimeters of over 3,000 Bulls indicated the following Classification of Bulls of all Breeds, except Brahmas.^{11,5,6}

Classification	Age In Months				Score*
	12-14	15-20	21-30	30+	
Very good—	> 34**	>36	>38	>39	40
Good—	30-34	31-36	32-38	33-39	24
Poor—	<30	<31	<32	<34	10
[Brahmas (average)—(Pre-pubertal)]	27-29	31-33	35-37]		

*Score designated for analysis of potential breeding ability in bull evaluation procedure for Society for Theriogenology.

**Centimeters (Scrotal tapes may be obtained from Lane Manuf. Inc., Denver Colo.)

As described previously in this Chapter the scrotal circumference of rams and the testis width and length in stallions is also closely correlated with their output of spermatozoa. The number of spermatozoa produced per gram of normal seminiferous tubules or testes is fairly constant for adult normal bulls since about 75 percent of the testis is composed of seminiferous tubules. For bulls over 6 years of age the scrotal circumference as an indicator of sperm cell production may be of limited value because of chronic testicular changes in older bulls.

A tonometer was developed that could objectively measure the consistency of the testes.¹⁷ This was highly correlated with semen quality tests. Normal testes have a firm "springy" tone. A soft or very firm consistency often was related to poor semen quality, testicular degeneration, fibrosis or atrophy.

An examination of the retractor penis muscle, the sigmoid flexure of the penis, and the external palpation of the sheath and penis should follow the examination of the testes and scrotum. Often a short or limited protrusion of the penis in bulls is associated with paunchiness or excessive obesity, a "dropped loin" on mounting and inability to copulate successfully. Any swelling, fibrous

tissue, abscesses, hematomas, growths or adhesions should be noted and their significance evaluated. The **Bos indicus** bulls or their crosses often have a very pendulous and long prepuce. These breeds and the polled breeds usually have a mild to moderate eversion of the prepuce with a predisposition to trauma, infection and frostbite.

Rectal examination of the accessory reproductive glands as well as other pelvic and abdominal organs is necessary in the physical examination of the male. This can readily be done with the hand and arm in the bull and stallion, and with the finger in the dog. In the boar and ram examination is difficult or impossible. In the large animals the pelvic urethra is noted as a firm round structure on the floor of the caudal portion of the pelvis. The Cowper's or bulbo-urethral glands are covered with muscle so they cannot be palpated but they are seldom diseased. In the bull and stallion the prostate gland is palpated as a thick transverse fibrous band of tissue around the urethra at the cranial end of the pelvic urethra and just caudal to the neck of the bladder and the ampullae and vesicular glands. These accessory reproductive glands are carefully palpated for their size, and consistency. Any abnormality is carefully recorded especially if a pathological process, inflammation, induration or abscess is noted by a thickening of the part, atrophy, or swelling of the organ, and if pain is produced on palpation. In severe inflammations extensive adhesions may be present. If one or a portion of one of the accessory glands, ampulla, or ductus deferens is missing or dilated a congenital anomaly is usually present. In the dog the size of the prostate can be noted. If the gland is asymmetrical an abscess, cyst or carcinoma should be suspected and confirmed. On palpation through the abdominal wall large prostatic cysts or a distended colon may be palpated if the prostate is hyperplastic. In rare cases in the dog a perineal hernia may be present associated with a hyperplastic prostate, and should be differentiated from a dilation or diverticulum of the rectum. In the bull and stallion the kidneys and other pelvic structures may also be examined for evidence of cystitis, nephritis, or possible tumors. Fat necrosis is rarely found in bulls.

Other diagnostic tests and examinations should be performed on valuable sires especially where herd records indicate that a venereal disease might be present. These tests have been described previously in this chapter, in Chapter 3 on abortion diseases or in chapters on infectious, reproductive and systemic diseases transmitted by coitus or by artificial insemination with infective semen. These tests would include the many serologic tests, fluorescent antibody tests, cultures of preputial mucus or semen or other special tests including tuberculin tests or tests for blood parasites, or autoimmune factors. Isola-

tion of all new acquired males for 4 to 8 weeks while tests for infectious, contagious or venereal diseases and the administration of effective vaccines are being conducted is a sound practice to prevent the introduction of diseases into a herd or band of females by newly acquired males.

SEMEN COLLECTION AND EXAMINATION

The third part of a careful examination of a male is the semen examination. This is of great diagnostic value in determining the cause, severity and degree of testicular or accessory gland pathology present, as well as being of value in estimating the male's fertility. There is usually a definite correlation between testicular pathology, disease of the reproductive tract and accessory glands and the semen characteristics and fertility. The techniques and procedures used in the semen examination of bulls, rams and humans are more accurate than in the other animals because more work, research and detailed observations have been made on these species. More work on the other species of animals is highly desirable and is being undertaken. From the many reports in humans, bulls, and rams and the less numerous reports in boars, stallions, dogs and tom cats, the same general principles are applicable in semen examinations of all species. Semen characteristics or quality usually remain rather constant and within narrow limits for nearly all ejaculates from each male over a period of months and even years. Due to acute, severe, adverse influences, semen quality may decline rather rapidly but improvement is slow and usually requires months for recovery to occur. Since it takes approximately 50 to 70 days for the development of mature sperm cells from spermatogonia until ejaculation, it is possible for acute testicular degeneration to be present in the testes yet the semen quality as it appears in the ejaculate to be fairly satisfactory. The diseased state or infertility may become evident in 2 to 6 weeks. Testicular biopsies are seldom indicated in domestic animals except in aforementioned situations since one or more semen samples usually accurately reflect the condition of the seminiferous tubules of the testes. Males with the highest quality or the lowest quality of semen and fertility on the initial examination usually have the same quality when they are re-examined, of no severe systemic disease or stress occurs before times of collection (See Semen Quality, Examination and Fertility^{5,7,80,81,123}). Be slow to condemn a male or give a poor prognosis based on a single semen examination revealing poor quality semen; especially if the male is young and immature, if the male has recently been se-

verely stressed or had an acute debilitating disease, if the male is very valuable, if the male has not ejaculated recently, or if his semen has been collected and examined under adverse conditions by untrained persons. The entire ejaculate should be examined and not just a portion of it such as the "tail end" sample taken from a stallion or other male as it dismounts. Usually bulls, rams and men with good to fair semen samples have good to excellent fertility; while males with poor to very poor semen samples are invariably infertile or sterile. (See Semen Quality Examination and Fertility.^{54b,60-63,80,81}) In stallions, boars and dogs where most of the ejaculate enters the uterus poor to very poor semen samples result in reduced fertility and small litter size in the latter, to occasional sterility. Completely sterile stallions are rare. If some motile, normal sperm cells are present in the ejaculate conception is possible in all species. Occasionally males with apparently normal-appearing, good quality semen samples may be incapable of producing conception. Therefore the examination of semen samples and the physical examination of the males as a means of evaluating fertility should be performed carefully and the result should be interpreted conservatively. If one criterion used to evaluate semen is poor, the sample should be graded poor or questionable because usually for satisfactory or good fertility all of the criteria must be satisfactory or good. Occasionally one poor criterion of semen quality maybe compensated for by a good criterion, for example, good motility and low concentration often result in fair conception rates.

The Collection of Semen for examination is practical and fairly easy in all species of male domestic animals except possibly the boar and cat, in which certain individuals may require general anesthesia and electroejaculation.

The Bull may have semen collected in several ways, but only two are of practical value for semen evaluation. The simplest and earliest method of semen collection was from the vagina, by means of a spoon or syringe with a long nozzle following a natural service. A speculum may be helpful in this method. This technique is unsatisfactory because the relatively small volume of semen is mixed with a large volume of vaginal mucus so this method was not suitable for the evaluation of semen quality.

The massage technique in the bull, first described in 1925⁷ as a means of obtaining semen for examination and artificial insemination, has been further described.^{3,11,23} This method is employed rather seldom because some skill and experience are necessary to massage the ampullae per rectum; some bulls respond poorly to the procedure, and semen collections are usually not as clean and contain many more bacteria than those pro-

duced by other methods because the semen passes through the prepuce and drips from the preputial hairs. For this latter reason it is necessary to carefully wash, rinse, and dry with a brush and cotton pledgets or a clean towel the prepuce and the preputial hairs and the region around the preputial opening with warm physiological saline solution or clean warm water. This washing, if combined with stroking of the sheath, may induce urination, which is desirable inasmuch as urine is toxic to spermatozoa and massage of the ampullae is likely to stimulate urination. The prepuce should be carefully doused with 250 to 500 ml. of a physiological saline solution to remove epithelial cells, smegma, and dirt. Sexual stimulation of the bull with a cow or another bull is helpful in obtaining a satisfactory semen sample. The bull should be handled quietly and kept relaxed. The operator, wearing a glove and sleeve, gently inserts his lubricated hand and forearm into the bull's rectum, emptying it of feces. The seminal vesicles are then gently massaged a few times with the fingers by backward and downward strokes toward the urethra and a cloudy fluid containing few if any spermatozoa is expelled. An assistant with a funnel and several test tubes collects the seminal fluid and semen as it drips from the preputial opening or penis. The ampullae are then massaged similarly in a slow, rhythmic manner. With the second finger between the ampullae and the third and fourth fingers on the outside of the ampullae, the ampullae are "stripped" of semen by pressure against the floor of the pelvis and then the pelvic urethra may be massaged. Sometimes the ejaculate is retained in the sigmoid flexure of the penis or in the proximal portion of the prepuce; therefore after massaging the ampullae, the S-curve of the penis should be straightened out. About 80 percent successful collections were reported in 100 attempts on 15 bulls.²³ Twenty one bulls were massaged 102 times and semen satisfactory for use in artificial insemination was collected with an average volume of 5.9 ml. with a slightly reduced concentration.¹¹ No injury or bleeding was produced. Fertility was equal to samples collected in the artificial vagina. If massaged regularly by the same operator most bulls usually become accustomed and conditioned to this procedure within 3 to 4 weeks and produce a good semen sample promptly at the time of each collection. The indications for using the massage technique are the same as in the electroejaculation technique, namely, in bulls that are impotent, unwilling, or are unable to copulate. Another author²² has described a method of gentle manual massage of the glans through the sheath wall to produce erection and ejaculation without restraint in gentle, calm bulls in a quiet isolated environment. In practice the massage technique on bulls is seldom used because

it required more skill and patience than the other collection procedures.

Electroejaculation in bulls has proven to be a practical, easy, rapid and routine technique, especially for range beef bulls.^{2,11,3,4,5,12,14,17,21,25} This technique was first described and extensively used in rams in 1936.¹⁶ Modifications to adapt this technique to bulls has been successful. The probe is inserted into the rectum after the feces have been removed. The probe is usually available in three sizes about 60, 75 and 95 mm. in diameter with longitudinal electrodes, 3 in number on its ventral surface, and these must be kept clean and lightly sanded for good contact.¹¹ The probe is about 30 to 35 cm. long. For best results the largest probe that can be inserted into the rectum should be used. No portion of the electrodes should contact the anus when the machine is in use.² The older instruments such as the Dzuik, Marden and Nicholson electroejaculators, the former with ring instead of longitudinal electrodes, have been improved to avoid excessive stimulation of the motor nerves to the rear limbs that often resulted in damage to muscles.^{4,5} The use of a modified sine wave instead of the pulse wave for electroejaculation of bulls has also improved the ease of electroejaculation of bulls.^{2,11,4,5,14} A man should stand behind the bull being ejaculated to prevent the expulsion of the probe. These various types and models of ejaculators for bulls, rams and possibly boars may be purchased commercially.* (See footnote.)

A technique of electroejaculation using a ring or hand electrodes either slipped over the first and third fingers of a rubber glove, or held by the hand over the region of the base of the penis and prostate gland or the posterior portion of the ampullae has been described.^{11,13,25} This technique was favored over the rectal probe by some veterinarians because the bull reacted more favorably and with less vigorous contractions of the muscles of the rear limbs and back and other undesirable side reactions than with the older 4 electrode probes. The newer 3 electrode probes largely avoid these reactions. Furthermore using the ring electrodes required two men to ejaculate and collect the semen and the man behind the bull applying the electrodes cannot observe the protrusion of the penis and whether ejaculation is occurring.^{3,4} The use of the finger electrodes has declined in recent years as results were not as uniformly successful as the results with the improved electroejaculators.

*3 Electrode probe, Lane Manufacturing Inc., Denver, Colo., and Nicholson Manufacturing Comp., Chicago, Ill., Marden Electronics Co., Bryan, Texas, Standard Precision Electronics Co., Denver Colo. (Battery operated) and Production Products Inc., Lyndale, Ave., Minneapolis, Minn.

It is highly desirable to place the bull in a solid stanchion or chute with a pipe or bar behind their stifles inasmuch as they tend to push forward. The front of the stanchion should be constructed so that the bull's shoulders push against supports and choking cannot occur. The footing should be good to prevent slipping. Injured bulls may require a squeeze chute or a sling to support the bull during semen collection. All bulls stiffen slightly and arch their back or "hunch," the anal sphincter contracts and clear seminal fluid dribbles from the sheath when the current is applied. Some bulls ejaculated with the rectal probe lean to one side or raise and extend one hind leg or rarely even both hind legs. This may be caused by the probe not being located on the midline and stimulating the sciatic or pelvic nerves. It may also be due to using too much power. With the newer improved models of electroejaculators these reactions are minimal. Care should be used to not apply the current until the electrodes are through the anus and in the rectum as this is painful to the bull. Occasionally a broken or exposed wire at the base of the probe will cause abnormal reactions especially noticeable on inserting the probe and applying the current. Although the actions of the bull may make this technique appear painful, it apparently is not; repeated electroejaculation do not create fear or resistance to entering the same stall. The different variations in bulls in response to electroejaculation have been described.^{11,17,26}

The preputial hairs may be clipped and adjacent area washed, rinsed and dried or the ventral abdomen may be brushed. Teasing or sexually-exciting bulls or a rectal examination of the accessory glands prior to electroejaculation greatly aids the collection of a good sample. To prevent cold shock to the sperm cells, a rubber cone from an artificial vagina with an attached glass or plastic vial is placed in a plastic bag containing warm water at 90 to 100° F. attached to a metal ring about 7.5 cm. in diameter with a long handle.¹⁴ The amount and consistency of the ejaculate can thus be observed as it is emitted. An artificial vagina may also be used to collect semen during electroejaculation. Although modifications in technique and procedures may be required in using electroejaculation on certain bulls, stimulation should begin at the lowest power settings especially in young bulls. Power or voltage within a power step is controlled by a variable-stimulator knob. This knob should be manipulated smoothly and fairly rapidly and full power within that power step should be approached gradually by turning the knob only part way initially until maximum power in that step is reached after 3 to 4 stimuli. Stimuli should be applied for 2 to 3 seconds with a short rest interval, when the knob is returned to zero, of only about one-

half to not over 1 second. Usually 5 to 10 stimuli are applied at each power step. Usually 9 to 14 stimuli are necessary to cause erection and protrusion of the penis and 9 to 20 to begin and 18 to 35 stimuli to complete ejaculation.^{11,5} A definite regular rhythm should be maintained during this procedure. Each bull must be treated as an individual and should be observed as the current is applied to assess his particular response. Only the amount of voltage or power needed to elicit the necessary responses and gently build up stimulation should be used in bulls and rams. About 90 percent of the bulls will erect, protrude their penis and ejaculate a representative semen sample with the rectal probe. As the penis becomes erect and the glans protrudes through the preputial orifice, more power or voltage is applied and nearly full erection occurs. With more power the clear seminal secretion becomes milky and opaque indicating ejaculation is occurring and the semen should be collected. Electroejaculation usually requires about 3 to 5 minutes to accomplish. If a bull fails to protrude his penis with stimulation, change the position of the rectal probe or exert forward pressure on the sigmoid flexure above the scrotum. Occasionally the tip of the glans will catch in the prepuce near the orifice. There may be a variation in effects of electroejaculation between bulls and from time to time in the same bull. In general young bulls respond better to electroejaculation and produce more normal ejaculates than do old bulls.

Too many early stimulations at a subejaculatory level will yield much accessory gland fluid but may make it difficult to obtain an ejaculation. Too rapid an increase may lead to resistance on the part of the bull or a pre-erection ejaculation and to contamination or loss of semen in the prepuce. Neither general nor local anesthesia nor tranquilization prevented normal electroejaculation.²⁸ Tranquilization may aid in protrusion of the penis. In some bulls excessive seminal fluid may be secreted during electroejaculation resulting in semen with a low concentration of sperm cells. Experienced operators of an electroejaculator can routinely produce ejaculates nearly similar in volume and concentration to ejaculates collected in the artificial vagina. However the concentration of spermatozoa was consistently higher in semen collected with the artificial vagina and volume was consistently greater in semen collected by electroejaculation.^{1,11,2,17} The conception rates of bulls from which ejaculates were collected electrically were the same as when the ejaculates were collected in an artificial vagina.^{5,27}

Electroejaculation has become a useful adjunct to the artificial vagina in artificial insemination stations by allowing routine collections from crippled bulls without

mounting. This is useful in utilizing injured bulls; and it can be used in cases of slow-breeding, impotent bulls. However, as pointed out previously impotency may be hereditary and perpetuating this condition may be detrimental to the breed. This technique has proven of great value to veterinarians for obtaining semen from beef bulls, unaccustomed to handling and to the use of the artificial vagina, for evaluating semen of bulls before the breeding season when they go on range with cows.^{1,17} It is doubtful if artificial insemination of cows with Brahman, Zebu or Santa Gertrudis semen would be possible without electroejaculation. The art of electroejaculating bulls can be mastered with practice. However certain bulls may not respond adequately and poor "semen" samples with oligospermia are obtained. In these bulls other collection techniques should be tried including the ring electrodes, the artificial vagina or massage of the internal genitalia. If an adequate sample cannot be obtained, the bull should not be classified as questionable or unsatisfactory.^{11,4} Since semen could be collected by electroejaculation in nearly 100 percent of the attempts, this technique is superior to others for obtaining semen from untrained or intractable bulls refusing to ejaculate into an artificial vagina.¹⁵

The artificial vagina is the method generally preferred and widely used for the collection of semen from dairy bulls and bulls in artificial insemination studs, and bulls on farms accustomed to being handled. Great care must be used in handling bulls as even fairly quiet ones can become dangerous in an instant. It is best to control them with two ropes, one fastened to a heavy nose ring, the other passing through the ring and tied around the horns. A metal bull staff is not safe for restraining a bull.¹⁹ By changing the mount, changing the environment, allowing sexual rest, teasing or "stewing," and other means, it will be found that there are relatively few bulls that cannot be kept in artificial service for many years. By the use of the artificial vagina a clean, complete ejaculate can usually be promptly obtained from properly trained bulls. The early models of the artificial vagina perfected by the Russians consisted of an artificial vagina which fitted inside the vagina of a cow or a dummy. The present widely-used artificial vagina is modeled after the Cambridge type that was developed in England.^{7,10} The vagina consists of a heavy rubber cylinder about 7 cm. in diameter and 35.5 cm. long for young bulls, and 42 cm. long for older bulls; this is fitted with an inner rubber liner. The longer winter-type artificial vagina is rather awkward and heavy and is seldom used except under farm conditions during the colder winter months.^{25b} A rough-surfaced thick inner rubber liner apparently is preferred by bulls to a smooth, thin liner. The liner is longer than the heavy rubber cylinder and

is turned back over the ends. There is usually a hole or valve in the heavy rubber cylinder for introducing and removing the hot water that is used to warm the vagina. The rubber liner is usually held in place by broad, flat, rubber bands. These should be tied to the vagina so that there is no danger of their slipping off and becoming fastened around the penis of the bull at the thrust of ejaculation and resulting in amputation of the penis if undetected. A short rubber cone containing a glass or plastic collecting tube for semen is fastened to one end of the artificial vagina and is covered with a warmed insulating jacket.

The proper pressure and warmth in the artificial vagina is obtained by filling the water jacket, or the space between the inner liner and the heavy rubber cylinder, about one-half to two-thirds full of water depending on the size of the bull's penis. The temperature of the water should be 125° to 180° F., 50 to 70° C. The colder the vagina and the outside temperature, the hotter should be the water that is added. At the time of collection the temperature inside the artificial vagina should be between 105° to 125° F. or 40° to 52° C.²⁰ Only a small amount of lubricant should be applied by means of a sterile glass rod to prevent an excess of lubricant mixing with semen. The lubricant can be a water-soluble lubricating jelly such as "K.Y." jelly, which is readily obtained commercially. If the temperature of the artificial vagina is too low, the bull usually fails to thrust and ejaculate; if it is too hot, some spermatozoa may be killed, or it may cause the bull pain and he may develop a temporary fear of this method of collection. The glass tube on the rubber cone may be protected from breakage in the summer by having a piece of flannel or a paper hand towel fastened over it and in the winter a warm flannel of several thicknesses, an old coat-sleeve, or a special, quilted jacket with an impervious covering closed at one end can be slipped over that end of the vagina to keep the rubber cone and the collecting tube warm and protect the latter from accidentally breaking when the sample is collected. If collection is delayed during cold weather, this jacket and tube should be held under the arm or in the coat of the operator to keep the collecting tube warm.

Either a cow, a bull or a steer that is trained and quiet may be used for a mount since metal or wooden dummies or phantoms even though they are heavily padded and covered by a hide, usually are not as satisfactory. If a bull is a slow-breeder, a cow in estrus is desirable, or a mount, either male or female, that is highly attractive to bulls should be used. Bulls or steers are most desirable especially in an A.I. stud in order to prevent the possible spread of disease if the bull were to accidentally breed the cow used as a mount.

A few quiet and well-mannered beef and dairy bulls have even been trained to breed an artificial vagina without mounting or even having another animal close. The bull is brushed and stroked along the back and sides, and then along the abdomen, sheath, and testicles. When the penis is extended from the prepuce by this stroking, an artificial vagina is applied and ejaculation occurs.

In artificial breeding studs all dairy bulls are teased before service to increase the total number of spermatozoa ejaculated. In slow breeding bulls this teasing prior to collection also makes mounting and ejaculation more prompt and rapid when the artificial vagina is heated and ready. The animal to be mounted is placed in a breeding rack or confined in a solid fence corner where the footing should be good to prevent slipping. The mount animal if not in estrus, should be restrained with a noselead to assist in its immobilization. The bull should be properly restrained by ropes to his nose ring so when he dismounts he does not attack the collector.¹⁹ The underline and preputial hairs of the bull are brushed clean and if necessary washed and dried. Cleanliness and hygienic practices in the collection of semen from bulls is important. The location for semen collection should be clean, dry, and free from dust, dirt, and mud. Douching the preputial cavity with a warm physiological saline solution prior to service is of questionable value in reducing the bacteria present in the semen.⁸

If the semen collector is right-handed, it is easier for him to work on the right side of the bull. As the bull mounts, the prepuce enclosing the erect penis is drawn sidewise toward the collector by the cupped fingers of the left hand, thus deflecting the penis from the vulvar region or escutcheon of the mount animal. The sheath and penis should not be grasped tightly with the thumb and fingers. If the protruded penis is grasped, the bull usually retracts the penis and dismounts. The tip of the glans penis is introduced into the end of the artificial vagina that is held alongside the buttocks of the cow and tilted downward and backward so that the water collects in the lower or "caudal" end and provides the needed pressure and warmth to stimulate ejaculation on intromission. Swedish workers prefer to hold the vagina against the buttocks or ischial tuberosities of the cow, aiding the direction of the glans penis by the fingers on the prepuce but letting the bull seek, find and thrust into the artificial vagina.¹⁵ The bull should be allowed to thrust its penis into the vagina, since this thrust is necessary for ejaculation. If the operator prematurely pushes the vagina over the erect and extended penis, most bulls will not ejaculate. After ejaculation the vagina should immediately be tipped in the opposite direction so that the semen will run into the collecting tube. If an excess of water has

been used, it may be necessary to draw off a portion of that water before all the semen can drain from the artificial vagina into the tube. A possible mishap from using an excess of water is to have the rubber liner burst or the rubber bands forced off at the time the penis is thrust into the vagina. If the latter happens, the rubber bands should be counted and penis should be examined. Some operators make a small nick or hole in the rubber collection cone to release air at the time of the thrust. For some bulls a heavy rubber band about 1-1/2 inches in diameter is placed around the liner, between it and the heavy rubber casing, at the open end of the vagina to provide more resistance to the entry of the penis and thus promote ejaculation.

Since sperm cells are killed or injured by toxic substances, it is necessary that all new rubber equipment which comes in contact with the semen be carefully cleaned and sterilized before using. New rubber equipment is often coated with a powder to prevent the rubber from sticking together. This powder or coating is often highly toxic to spermatozoa. After each collection the cone and rubber liner should be rinsed immediately in warm water. All glass, metal, and rubber equipment should be washed and brushed with a lukewarm solution of 0.2 to 0.3 percent sodium hexametaphosphate such as "Calgon," or .3 to .5 percent tetrasodium pyrophosphate, or a good glass cleaner and rinsed thoroughly with warm water. The synthetic organic detergents should not be used in washing and sterilizing artificial insemination equipment.¹⁰ If they are used, very careful rinsing is necessary. After draining, all parts of the equipment are then rinsed in 70 percent ethyl alcohol and permitted to dry in a dust-free, ventilated storage cabinet. Other types of alcohol such as methyl or denatured should not be used. Some workers use a final rinse of scalding distilled water, followed by a rinse in 70-percent ethyl alcohol. The drying may be aided by replacing the liners on the vagina but a better procedure is to distend the rubber liner with ordinary clothes pins or a special metal rack. If equipment must be used before it has dried, the alcohol should be thoroughly washed away with physiological saline or a sterile citrate- or phosphate-buffer solution. The artificial vagina may be sterilized by boiling or by being placed in an autoclave but this hastens deterioration of the rubber parts.

The artificial vagina method for the collection of bovine semen produces a clean concentrated semen sample with cheap, simple equipment and provides information on sex drive. It has the disadvantages of requiring a relatively trained cooperative bull and a suitable mount. The danger of injury of the operator is greater. While the electroejaculation method of collection gives good re-

sults with few specialized facilities and even with untrained bulls, it has the disadvantages of requiring more costly equipment, a greater chance of a contaminated sample with a low concentration of spermatozoa being collected, and no indication or determination of the sex drive, libido or ability to mount and ejaculate, or freedom from lameness, of the bull is obtainable.

The stallion may have his semen collected relatively easily by using a condom,⁹ or by the use of the artificial vagina.^{2,3,8,14} The former method is seldom used at present because of the excessive contamination of the ejaculate by the penile skin.

The collection of semen from the vagina or uterus of the mare after natural service is possible and has been described.⁴ However samples collected in this manner are not representative, are diluted and possibly contaminated. This technique requires that the mare be healthy and free of any genital infection and not be in her foal heat. Strict hygienic and sanitary procedures should be followed in the collection of the semen by this method. After service by the stallion the hand encased in a sterile glove and sleeve is introduced into the vagina with a stiff rubber tube 3/16 inch in diameter and about 2 to 2-1/2 feet long. This tube is attached by a bent glass tube in a 2-holer rubber stopper to a 6-ounce sterile bottle and a 12- to 18-inch tube is similarly attached by a glass tube in the other hole of the stopper. By suction applied on the short tube with the mouth, semen is drawn into the bottle from the vagina and if necessary from the uterus. Another but less satisfactory method is to use a vaginal speculum and draw up the semen with a long nozzle attached to a syringe. These techniques are presently seldom used.

Collection of the "dismount" or "tail-end" sample of stallion semen that drips from the glans and urethra after copulation can be easily accomplished by holding a warm enamel or plastic cup or large plastic funnel attached to a warmed tube or bottle under the vulva and glans penis as the stallion dismounts. This last portion of the ejaculate has a much lower concentration of spermatozoa, has a different composition than the complete ejaculate, and is usually unsuited for predicting fertility and for inseminating purposes.⁹ The amount of semen collected in this manner is small, 10 to 30 ml., and it is commonly contaminated with smegma and dirt. Collection and examination of this "tail-end" sample is usually performed to be certain that ejaculation occurred during intromission. Semen collected in this manner, is usually filtered through sterile gauze or a coarse-paper or milk filter into a vial before it is used for insemination or "impregnation" following a natural service.

Massage of the ampullae and electroejaculation as described in bulls has been attempted in stallions without success by the author and others.⁵ With the horse completely anesthetized electroejaculation is possible, as reported in swine, but it is not practical and urine often contaminated the sample.¹ These above techniques, for obvious reasons, are not as satisfactory as collecting the entire ejaculate in an artificial vagina.

The condom or breeder's bag was used successfully on most Thoroughbred stallions.^{9*} A mare in estrus, a mare that has been given 10 to 20 mg. of stilbestrol 24 to 48 hours previously to produce signs of estrus, or a very docile, trained older mare can be used with the usual restraints as a mount.

A satisfactory condom for the stallion similar to that used by man was designed. Before use the breeder's bag or condom should be thoroughly cleaned of all rubber preserving powder by thorough washing, rinsing with plain or distilled water and then rinsing with a physiological salt solution. If the condom is to be reused it should be sterilized after washing and rinsing by immersing in ethyl alcohol and dried. Before applying the condom the penis should be carefully washed and rinsed thoroughly several times with plain water and dried to remove dirt and smegma. The condom is fitted to the erect penis, but the left loose over the glans with the air squeezed out, just prior to service. It is held in place by rubber bands and removed immediately after service. If an excess of fluid collects in the condom before ejaculation empty it out. The ejaculate is poured into a sterile bottle or graduate warmed to about 100 to 102° F. Lubricating the outside of the breeder's bag and vulva was not necessary if the stronger condoms were used. As previously indicated this technique is seldom employed at the present time because nearly all stallions can be readily trained to ejaculate into an artificial vagina.

The artificial vagina has been widely used in England, Russia, Japan, and the United States for the collection of semen from stallions. When this is performed regularly the stallion may be trained in its use. The artificial vagina is preferred to the condom because of more satisfactory results and less contaminated samples.^{11,2,3,4,6,8,12} The equipment, however, is more expensive. Some stallions that are collected regularly have been trained to mount dummies, manikins or phantoms.^{7,10,11} A mare in estrus or one in which estrus has been induced, is usually required. Strict hygienic pro-

*Condoms for stallions may be purchased from the Pioneer Rubber Co., Willard, Ohio, Youngs Rubber Co., Trenton, N.J. and Dean Rubber Co., East Kansas City, Mo. (Texas Model.)

cedures should be followed, such as: bandaging the mare's tail with a sterile bandage; careful and thorough washing, disinfection and rinsing of her rear parts; and careful washing and rinsing of penis and sheath of the stallion. The usual precautions are taken to restrain the mare and to prevent injury to the stallion, the operator, or the mare.^{11,6}

The method of constructing the Missouri-USDA type of vagina has been described.^{*4} The Mississippi model has been described by Berliner.³ Lighter more modern artificial vaginas for stallions are also available.^{**} The diameter of the vagina is about 12.7 to 17.7 cm., 5 to 7 inches, and because of its increased size and weight a handle is provided. A dam is present at the closed end of the Nishikawa (Japanese)¹² vagina that provides a place for contact for the glans penis. An equine artificial vagina has been designed and used successfully for many years in Colorado.^{***11} The outer casing is made from a nalgene pipette jar using rubber tubing similar to a bovine artificial vagina and the vagina is well-insulated. A built-in filter is provided that removes the gel from the ejaculate. A new vagina must be thoroughly washed, rinsed, disinfected with grain alcohol, and dried before it is first used, and following each use thereafter. The water-soluble lubricating jellies can be used sparingly to lubricate the opening of the vagina. The temperature of the vagina should be between 105 to 120° F. or 43 to 50° C. Temperature within a degree or two of 46° C. is desirable. This is provided by introducing hot water at 120° to 130° F. or 50 to 65° C., depending on the climatic conditions, between the jacket and the liner of the artificial vagina. Pressure in the artificial vagina simulating that of a mare's vulva may be produced by a 2 inch wide rubber band, 3 inches in diameter, placed between the jacket and the rubber liner near the open end of the vagina. Berliner advised manual pressure through the wall of the vagina. Some of the artificial vaginas such as the Japanese and Colorado types have rigid outside walls. Air and water can be introduced into the artificial vagina to produce adequate pressure on the penis. Although the operator may collect semen from either side of the stallion, most prefer the left or near side. The site

for collection should be level and provide good footing. The artificial vagina should not be shoved over the stallion's penis as he mounts but rather the stallion should be permitted with help to insert his penis into the vagina. On cold days the bottle receiving the semen should be warmed and protected. The vagina should be held firmly against the flank and buttock of the mare with the open end of the vagina held above the level of the plastic collecting bottle and pressure exerted against the penis equal to that exerted by the stallion. It usually requires about 20 to 30 seconds for ejaculation. The operator can place his fingers on the ventral surface of the caudal portion of the erect penis, to detect the pulsations of the urethra during ejaculation.^{11,6} If the stallion or jack is not properly trained or lacks desire, a quiet mare or jenny and quiet surroundings are necessary for collection with an artificial vagina. The author has successfully used a bovine artificial vagina for the collection of semen from small ponies. Stallions that require repeated intromissions before ejaculation or are slow to mount and copulate at natural coitus act similarly when semen is collected by the artificial vagina.

Patience and gentle training may be required, particularly if a stallion is to be collected on a phantom.^{7,10,11} The use of a phantom eliminates most of the possibilities for injury to the mare, stallion and collector. Because of the lower height of the phantom and its immobility it is less stressful to the rear quarters of the stallion. The use of urine from an estrous mare on the phantom is of questionable value as a sexual stimulant to the stallion.¹⁰

The ram and buck may have satisfactory semen samples collected by removing the semen from the vagina of a ewe after coitus, by an artificial vagina or by electroejaculation.

Rams may be mated to restrained diestral ewes. The ewes' vaginas are cleaned prior to use by repeatedly inserting and withdrawing saline with a collecting pipette of glass or plastic 30 cm. long and 1.0 cm. in diameter attached to a syringe until no more mucus can be removed. If the ram refuses to breed a diestral ewe, one in estrum may be used. After coitus semen is removed in a similar fashion. This is a simple method but the semen is usually contaminated. It is faster for collecting from shy, untrained rams than the artificial vagina method and it also detects rams that physically are unable to copulate. Semen evaluation can be performed satisfactorily on such samples.^{4,11}

The artificial vagina for rams and bucks is constructed like the artificial vagina for bulls but it is smaller, about 20 cm. long and 5 cm. in diameter. The temperature of the vagina at the time of collection is critical for

*Haver-Lockhart Laboratories, P.O. Box 390, Shawnee, Mission, Kan., 66202.

**Artificial Vagina for obtaining stallion semen (Nishikawa Model) Fukihira Industry, Co. Ltd., 131 Morikawa-Cho, Bunkujoku, Tokyo, Japan, Goetze's Artificial Vagina for Horses, H. Hauptner, Solingen, Germany.

***Colorado Equine Artificial Vagina, Lane Manuf., Co., 2057 S. Hudson St., Denver, Colo., 80222.

the ram and should be 41° to 44° C. or 106° to 112° F., with a pressure of 40 to 60 mm. of mercury.^{7,8,9,10} Rams and bucks may be readily trained in a suitable environment, with a restrained ewe or doe preferably in estrum. Later any ewe or doe, an ovariectomized ewe or doe treated with estrogen, or even a dummy may be used as a mount. As the operator holds the vagina in his hand he should be crouched next to the rear parts of the ewe and doe and be alert as mounting and copulation is very rapid. False mounts without ejaculation are common. The penis should not be touched by the hand but the sheath may be grasped to direct the penis into the artificial vagina. A refractory period of 20 to 30 minutes follows ejaculation in the ram and buck before he will mount again. A ram or buck may be collected 2 to 3 times a day for a number of days.

Electroejaculation of rams was first described by Gunn in 1936.³ In recent years improved electroejaculators are available with bipolar rectal probes about 30 cm. long and 2 cm., in diameter.* (See footnote.) The ram responds rapidly to electrical stimulation and often 3 to 5 stimulations of 3 to 5 seconds duration with 1 to 2 seconds rest, at 2, 5 and 8 volt peaks result in ejaculation.^{1,2,5,12}

Thus fewer stimulations by the electroejaculator are needed in rams and bucks than in bulls. The insertion of the rectal probe to a depth of 15 cm. instead of 20 to 25 cm., improved the rapidity of response and produced a greater volume of semen. Rams and bucks may be electroejaculated in the standing position or restrained on their side with their legs extended. The latter position is more often recommended. The penis should be removed from the sheath and held with gauze so the urethral process is directed into the collection vial or tube to avoid ejaculation into the sheath. Often the penis will protrude from the sheath with electrical stimulation as in the bull. This method results in a great variation in semen volume and lower concentration than an ejaculate collected with the artificial vagina. Occasionally urine may contaminate the sample. If the first collection is unsatisfactory it is difficult to get another satisfactory ejaculate until several hours have elapsed. Electroejaculation has the advantages that it may be used on untrained rams and bucks and is particularly valuable as a screening test of the semen quality of large numbers of rams.^{2,5} Indiscriminate use of electroejaculation without re-examinations could

lead to the culling of many potential high fertility rams as occasional samples of semen obtained by electroejaculation from fertile rams and bucks were inferior in quality. The induction of erection and ejaculation in rams and bucks by the local massage of the sheath and penis has been described.⁶

The boar may have semen collected by a modified artificial vagina, the gloved-hand technique or by electroejaculation. Before collection by any of these procedures the contents of the preputial diverticulum should be expelled and the area of the preputial orifice should be cleansed and dried.

The artificial vagina may be of various designs to provide the necessary pressure to the spiraled glans penis so that it "locks" at complete erection as it does in the anterior vaginal and cervical folds of the sow. This may be accomplished most simply by a heavy rubber casing 4.5 cm. in diameter and about 12.5 cm. long with a rubber liner and small piece of sponge rubber between it and the casing where warm water at 45° to 50° C. or 113 to 122° F., is placed to heat the vagina. The sponge rubber causes increased pressure on the penis. A continuous, smooth, thin rubber liner or tubing 40 cm. long and 3 to 3.5 cm. in diameter with a small hole in the upper portion to allow air to escape is passed through the above vagina and fastened to the outer end of the vagina and lubricated. The other end is fastened to a plastic bottle or bag of 500 ml. capacity that is in a cup or thermos of warm water at 102° F. or 39° C. As the penis passes through the vagina pressure is applied to the glans by the hand of the operator through the thin rubber tubing.^{4,6,9,10} After several back and forth motions the penis "locks" in the fingers, continuous moderate pressure is applied, and ejaculation commences and continues for about 15 minutes with much of the sperm-rich fraction being emitted around the third or fourth minute. This is a somewhat similar procedure to the gloved-hand technique but more cumbersome. Frequently there may be a series of sperm-rich fractions interspersed between periods of thin sperm-poor fractions and gelatinous tapioca-like secretions. A slightly more complex model of artificial vagina the diameter of the artificial vagina for the bull, but only 18 cm. long designed to prevent contamination of semen with preputial secretions has been described.^{10,11} A very simple model consisting of only a 35 to 40 cm. rubber tubing as described above with a key ring for an orifice that is warmed before use has also been described.^{5b} Other earlier types were similar to the artificial vagina for the bull but with attachments to it so air could be pulsed into the vagina.^{2,11}

Currently most workers collect semen from boars with only a gloved hand and a wide-mouthed thermos jug

*Nicholson Manufacturing Inc., Chicago, Ill. Production Products, Inc., (Dzuik Model) 4607 Lyndale Ave. N., Minneapolis, Minn., Lane Manufacturing Co., Hudson St., Denver, Colo. Marden Electronics Co., Bryan, Texas. Standard Precision Electronics Co., Denver, Colo., (Battery operated).

containing warm water and lined with a plastic bag to prevent chilling of the semen. This technique is easy, inexpensive, and repeatable.^{7,8} After the boar mounts the estrous or restrained sow and protrudes the penis, the hand, encased in a surgical glove, is shaped like a cone to permit the entry of the glans penis and placed several inches cranial to the preputial orifice. After the penis enters the hand the fingers are gently closed locking the spiral penis in the hand. It is critical that the distal 2 to 3 centimeters of the penis be held quite firmly with the small, fourth, and third fingers with no pressure applied to the shaft of the penis. Full erection then occurs and ejaculation follows.⁸ The mouth of thermos jug may be covered with several layers of gauze or cheesecloth to separate the gel fractions from the rest of the semen. Usually ejaculation takes about 5 to 15 minutes and occasionally some boars will have a second ejaculatory cycle, shorter than the first, before dismounting.

Boars are usually readily trained to mount a dummy composed of a metal or wooden frame covered with burlap or they may be allowed to mount a confined or restrained sow or barrow. The former is preferable. The environment should be quiet and the footing non-slippery.^{7,10,6}

Electroejaculation in boars has been described.^{3,5a,b} It is not as desirable as the gloved-hand or artificial vagina for the collection of semen because mating behavior and ability to mate cannot be assessed and the procedure and equipment is costly and the ejaculate secured is not typical. The older Dzuik model or newer small bull or large ram probe is satisfactory if the rectum is evacuated of feces before the probe is inserted. Stimuli must be applied at gradually increasing voltage peaks in a rhythmical manner similar to the technique used in bulls to first induce erection and then by inserting the probe an additional 6 to 8 cm. into the rectum to produce ejaculation. The volume of semen obtained is low but the concentration is usually high because of a lack of accessory gland secretions. Since boars must be forcibly restrained, the collection is a noisy drawn-out affair, often resulting in a heavily contaminated ejaculate. The electroejaculation of boars is not as satisfactory as in bulls and rams. For this reason the electroejaculator should be used on anesthetized boars. One to one and one-half grams of "Surital," sodium thiamylal (Parke-Davis) given intravenously in the ear vein through a 20 gauge needle produced good anesthesia for 15 to 30 minutes in 300 to 400 pound boars.^{3,5a} The genital organs were easily and thoroughly cleansed and the penis was removed from the prepuce by the fingers or by gentle traction with forceps while the initial electroejaculating stimuli are applied resulting in erection. The penis was held by the hand and

directed so the semen would flow into a warmed thermos jug lined with a plastic bag when ejaculation occurred. Under anesthesia the penis and testes are easily examined. The above method was rapid and quiet and was preferred³ for the evaluation of the semen of boars to the use of the artificial vagina which required obtaining sows in estrus or training the boar to mount and use the artificial vagina. Shy, slow, inexperienced, mean, lame or injured boars are difficult to train. Training procedures can't be standardized and are very time consuming. If a live mount is used there may be disease control problems to consider.

In the dog semen may be obtained for examination or artificial insemination by digital manipulation of the penis or by an artificial vagina. A method of electroejaculation of the anesthetized dog modeled after the procedure in rams has been described.¹ This proved useful in a very few males that could not be collected by the former two methods. Most untrained dogs respond best to digital manipulation.^{6a,11,3,7,8,11}

The collection area should be a small quiet room with minimal distractions. The dogs and teaser bitch should be handled quietly after they have become acquainted with the operators and the collection room. The footing should be nonslippery. The teaser bitch is usually fastened securely to a table leg or wall and held by an assistant with a hand under her chest and the other hand around her muzzle to prevent her from sitting down or possibly biting the male or the operator.

Manipulation of the base of the penis is the simplest, cheapest, and commonest way to collect semen in the dog. A bitch, preferably in heat, should be presented to the male. When the dog shows sexual interest the preputial skin is pushed caudally, exposing one to two inches of the glans penis. The base of the penis behind the bulbus glandis is grasped through the prepuce and moderate pressure is applied by the fingers. In an impotent male back and forth movement, masturbation, may aid in producing an erection. As erection occurs the prepuce is retracted behind the bulbus glandis and digital pressure is maintained caudal to the bulbus to simulate its engagement in the vulva. The dog during ejaculation will often step over the arm of the operator causing the penis to be extended caudally between the dog's rear legs as he faces the opposite direction. Even though no teaser bitch is present some dogs can be trained to ejaculate by manipulation of the base of the penis until erection is induced, but sperm cell concentration is usually low.

The semen is collected by means of a warm glass or plastic funnel into a 25 to 30 ml. warm tube or vial or the warmed barrel of a 20 to 50 ml. plastic or glass syringe on which a rubber adapter has been placed and

doubled over to prevent leakage of semen. Since glass collection equipment is difficult to handle with an active, thrusting dog and may break or traumatize the penis, a collection apparatus consisting of a rubber conical sheath, similar to the conical sheath used on a bovine artificial vagina but cut down or folded at the large end to reduce its size with a 15 ml. conical plastic centrifuge tube placed in the narrow end of the rubber sheath and warmed to 38 to 40° C. also prevents loss of semen during ejaculation.¹¹ A very small amount of K.Y. jelly may be applied to the inside of the rubber sheath. The first portion of the ejaculate may be lost due to a brief period of thrusting motions by the male. This is of little importance, as few spermatozoa are present in this portion. When the ejaculation of sperm cells commences thrusting motions cease. The penis does not need to enter the tube or syringe barrel and in shy or impotent males the funnel, tube or syringe barrel should not be allowed to touch the penis. It is important to maintain constant pressure behind the bulbous glandis until sufficient semen has been collected.^{6a,7,10,11,2,7,8,11} The portion of the ejaculate containing the spermatozoa is a whitish-grey milky fluid. Ejaculatory action can be noted by feeling the pulsations of the urethra in the base of the penis. Ejaculation may last 5 to 15 minutes.

An artificial vagina for the dog similar in size, 5 cm. in diameter and 19 cm. long, and similar in pattern to the artificial vagina for a ram has been described.^{4,5,6,9} A firm rubber diaphragm around the open end of the vagina to simulate a bitch's vulva was recommended.⁴ The temperature of the vagina should be about 40° to 42° C. or 104° to 107° F., and no lubricant need be used. The penis is grasped behind the bulbous glandis as described above to produce erection before the vagina is applied. Semen motility may be adversely affected by this technique.² Possibly this was due to the contact of the sperm cells with the heated walls of the artificial vagina as this finding was not reported by others that used and preferred an artificial vagina for semen collection in the dog.

In the tom cat semen collection has been described by the use of the artificial vagina¹² or by electroejaculation under anesthesia.¹⁰ Male cats were selected for their calm temperament and for their strong libido. Teaser queens were either females in estrus or ovariectomized females given 12.5 mg diethylstilbestrol, **Repositol**, every 10 days. It usually required about 2 weeks to train a tom cat for routine semen collection. The artificial vagina was a 2 ml. rubber bulb from the end of a bulb pipette or "eye dropper" with the bulb end cut off and fitted over a 3 × 44 mm. test tube. This was placed in a 60 ml. plastic polyethylene bottle. The bottle

was filled with water at 52° C so at the time of collection the temperature would be 44 to 46° C. The open end of the rubber bulb was rolled over the mouth of the bottle and smeared lightly with K.Y. jelly. The artificial vagina was slipped over the penis of the tom as he mounted the teaser queen and developed an erection. The operators other hand was used to steady the tom and teaser queen. Collection took from 1 to 4 minutes. Their study indicated that toms could be collected 3 times a week and daily use for a short period was possible without a great decline in semen quality. Daily collection did not affect the male cats' libido. The electroejaculation procedure required special equipment and rectal probe and after anesthesia was induced with Ketamine HCL the technique was similar to that used in the other domestic animals with a similar response.¹⁰

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SEMEN QUALITY EXAMINATION AND FERTILITY ASSESSMENT

Examinations for semen quality can only be satisfactorily performed on approximately normal ejaculates within a short period after collection. The ejaculates must be properly protected and handled until examined. Some factors to consider in the proper handling of semen are: (1) The artificial vagina or the container used for semen in electroejaculation should be clean and free from con-

taminants that might injure spermatozoa, such as: alcohol, excessive petrolatum, powder present on new rubber liners, and antiseptics or chemicals of any kind; (2) at the time of collection excessive dirt or debris including preputial smegma and secretions should be kept out of the vagina; water and urine injure spermatozoa by creating a different osmotic pressure; (3) excessive amounts of blood and serum may adversely affect spermatozoa; (4) overheating and too-rapid chilling injure spermatozoa, (5) too much agitation and shaking of the semen damages spermatozoa; and (6) excessive exposure to sunlight should be avoided. It is important that the semen sample be examined as soon as possible after collection.⁷⁰

A good laboratory with the necessary very clean glassware and equipment and a well-trained technician, if it is within a few hours drive is the logical place to have the semen examination performed. However, all too often a semen sample is sent to a laboratory at some distance; and the motility and other qualities may be so affected during shipment that the value of such an examination is questionable or limited. In many of these instances only a morphological examination and density estimation of spermatozoa can be performed. Usually a warm "laboratory" at 60 to 80° F. can be set up in an automobile with a good heater. Portable electric incubators that can be connected to a 110 volt circuit are now available for the warming of equipment. For this reason the author firmly believes that by the use of a microscope most trained veterinarians can perform by means of a few simple laboratory procedures on the farm or ranch 3 or 4 semen tests on a male and more accurately determine his probable fertility than can a trained laboratory technician receiving a single ejaculate by mail. The veterinarian also has access to the complete breeding history, information on the male's sexual desire and frequency of service, and other pertinent information, such as his performance during copulation, from a careful physical examination not known to a laboratory. In this testing procedure as in other laboratory techniques the results must be carefully evaluated on the basis of the information obtained and what is known concerning the case; too much reliance should not be placed on the results of tests on a single ejaculate of semen. The best fertility evaluation test is the conception rate of the females bred to the male. Semen examinations, if carefully done, may provide a ready and reasonably accurate measure of whether the male is probably fertile or definitely infertile and be of value in determining the severity and the possible cause of infertility affecting a male. If special staining techniques, electron microscopy or other complicated procedures are necessary for morphological

studies on certain semen samples these must be done in specialized laboratories under the supervision of skilled and knowledgeable technicians and scientists.

Semen quality of the first ejaculate after a long period of sexual rest may have a lowered motility and an increased number of dead spermatozoa. Semen quality in many rams and a few bulls may be decreased during the hot summer months. Season of the year had a significant effect on semen quality in stallions with the best quality of semen produced late in the spring or early summer and the poorest quality semen in the winter months.^{94,95,96} Similar conditions prevail in the breeding and nonbreeding season of sheep and goats. The various common tests on semen are as follows:

Volume—The usual volume of the ejaculate in the various domestic animals has been noted previously. Repeated frequent ejaculations may temporarily lower the volume of the ejaculate. However, under the usual breeding conditions the amount of the ejaculate produced remains fairly constant for each species of animal. (See Table 21.) Under conditions of artificial insemination, teasing or "stewing" of bulls, dogs, boars and other species is often practiced to increase the numbers of spermatozoa and possibly the volume of the ejaculate. Restraining bulls for 2 to 5 minutes or more to induce sexual excitement before allowing ejaculation, was accompanied by increases of about 40 percent in the number of motile spermatozoa per ejaculate over unrestrained bulls.³¹ Small volumes of semen may be ejaculated in young males, in males used excessively, in incomplete ejaculation or failure of ejaculation, and in cases of bilateral seminal vesiculitis in bulls and stallions. An increase or decrease in volume of semen ejaculated is usually not correlated with fertility in a male unless ejaculation fails to occur.

Color—As described previously ram and bull semen is concentrated and the color is milky or creamy white and opaque. (See Tables 23 and 26.) It is normally like cream in consistency. In the stallion, boar, and dog the spermatozoa are much less concentrated and the color is pearly-white to grey and translucent. A creamy consistency of semen is present in bulls with spermatozoan concentrations of 1,000,000 to 1,200,000 per cmm. or higher; a thin milky consistency with spermatozoan concentrations of 500,000 to 600,000 per cmm., and watery, translucent or clear semen occurs with fewer than 300,000 spermatozoa per cmm.⁵³ Brownish-colored semen in bulls, probably due to blood pigment, may be observed in cases of orchitis.³⁶ The light yellow color seen occasionally in the semen of some bulls at the time of collection is due to riboflavin secreted by the accessory glands and it has no significance.

The presence of *Ps. aeruginosa* in bull semen may cause a change from a normal to a yellowish-green color when semen is left standing at room temperature.⁵³ Clumps, clots or large flakes in semen are due to the presence of pus usually from the accessory glands or ampullae. A dark red to pink color of the semen is due to the presence of varying amounts of blood from the genital tract, urethra or penis. A light brown color may be due to the presence of feces in the semen. When the semen is not a normal color and consistency, further examination should be made of the actual density or concentration of the spermatozoa, since reduced fertility may accompany a reduced or low concentration of spermatozoa or severe contamination with substances or agents harmful to spermatozoa.

Hydrogen ion concentration or pH value of the semen of domestic animals has been reported previously. Measurements of the pH of semen at the time of collection is of little practical value in the normal male for predicting fertility.^{7,114} In bulls, rams and dogs the pH of semen is neutral, about 6.7. A pH of 7.0 or higher in semen was observed in bulls used excessively, in incomplete ejaculates and in pathological or inflammatory conditions affecting the testes, epididymides, ampullae or vesicular glands.²⁰ The semen of stallions, boars and cats is normally slightly alkaline in reaction, pH 7.4. First ejaculates from stallions had an average pH of 7.47 and second ejaculates collected soon after the first were more alkaline, pH from 7.5 to 8.0.^{94,95} The pH of semen may be measured with pH paper, with bromthymol blue or a pH meter. When an inflammatory condition affecting an accessory genital organ is suspected or present and characterized by an elevation of the pH of the ejaculate, a catalase test is indicated. High catalase activity of semen, a reaction greater than 300 on the tube used for the test, is demonstrable in cases of acute seminal vesiculitis of bulls.

Concentration or density of spermatozoa in semen has been cited previously for the various domestic animals. (See Table 23.) The concentration of spermatozoa in ejaculates of fertile bulls varies from 300,000 to 2,000,000 per cmm. with an average of 800,000.⁷⁴ Ejaculates collected with the electroejaculator frequently have a lower concentration and a greater volume than those collected with the artificial vagina due to an excess of accessory gland secretion. Spermatozoan density is within normal limits in many bulls with testicular degeneration and therefore other tests are usually necessary for an accurate evaluation of semen quality.⁵³ It was indicated that concentrations of spermatozoa below 600,000 should be looked upon with suspicion. In 24 bulls with serious affections of the testes, 13 had oligospermia, fewer than

200,000 spermatozoa per cmm. and 7 of these had fewer than 10,000 spermatozoa per ml.^{16,20}

Some watery translucent ejaculates in bulls were due to incomplete ejaculation.^{16,20,108} In humans low concentrations usually were correlated with infertility but exceptions were common.⁸⁰ In fertile men with low sperm cell counts the motility and morphology of the spermatozoa were good. In general, however, there was a definite correlation between spermatozoan density, motility, and morphology. In rams⁵⁰ and boars⁵⁸ testicular degeneration is characterized by a marked decrease in the spermatozoan concentration correlating with the severity of the degeneration. As reported previously, spermatozoan concentration is usually very low, less than 75,000 per cmm., in testicular hypoplasia of bulls with complete or nearly complete sterility.^{53,74} Another characteristic of sperm cell concentration noted in many infertile or sterile bulls was the rapid decrease in spermatozoan concentration between the first, second, and third successive ejaculates, indicating poor spermatozoan reserves and reduced sperm cell production.^{53,99} Fertility declined in stallions when there were fewer than 2 billion spermatozoa in the ejaculate.³⁵ The incidence of azoospermia or oligospermia in several thousand stallions examined was low, 0.04 to 0.14 percent.^{12,13} Fertility usually depends upon the total number of actively motile normal spermatozoa in the ejaculate.

The techniques used for determining concentration of spermatozoa are as follows:

1. The color or macroscopic examination of semen in bulls and rams with concentrated semen is quite satisfactory for an approximation of the density of spermatozoa. (See Table 26.) In boars, stallions, and dogs gross examination of semen is not accurate even with the ge-

Table 26. Sperm Cell Concentration and Semen Color in Bulls and Rams

Bulls (per cmm)	Rams (per cmm)*	Color of Semen
	2,500,000	Thick, creamy
2,000,000	2,000,000	Creamy
1,000,000	1,000,000	Light creamy
500,000	500,000	Milky
100,000	100,000	Cloudy, watery, translucent
less than 50,000	less than 50,000	Almost clear, transparent, watery

*Gunn and coworkers.⁵⁰

latinous portion of the ejaculate of stallions and boars removed. Although as the examiner gains experience this method will give a fair indication of the spermatozoan concentrations in the more concentrated samples in bulls and rams; but in medium to lower ranges the visual estimation of sperm cell concentration is subject to serious errors.

2. The enumeration of spermatozoa may be made with a hemocytometer in a manner similar to that used in making a red blood cell count.³⁰

One procedure was to fill a red blood-cell pipette to the 0.5 mark with undiluted semen. A 3 percent chlorazene solution was drawn up to the 1.01-mark in the pipette; this diluted the semen and killed the spermatozoa. This mixture was shaken carefully but vigorously for 2 to 3 minutes. A few drops were released and the shaking was repeated. A few more drops were released and then a drop was placed under the cover slip in a Neubauer blood-cell counting chamber. Sperm cells in 5 large squares were counted in a diagonal direction and the total number of spermatozoa counted were multiplied by 10,000.¹⁰⁵ This procedure rapidly gives an accurate indication of the sperm cell concentration per cmm if the mixing is thorough.

3. The concentration of spermatozoa may be obtained rapidly in a well-equipped laboratory by a photoelectric colorimeter that has previously been properly calibrated by known spermatozoan concentrations.¹²¹ After adding 1 part bovine semen to 40 parts of sodium citrate buffer, the diluted semen is placed in a special tube in the photometer. By reading the dial on the photometer and comparing this reading with a chart containing previous readings with known spermatozoan concentrations, the sperm cell concentration of the ejaculate in question can be determined very rapidly. This may be adapted to dogs or other species. In the dog a dilution rate of 1 to 4 to 1 to 16 was recommended.⁴³

This technique is used in most bovine artificial breeding laboratories for determining the concentration of spermatozoa. This information is necessary for computing the dilution or extension factor.

4. The comparing chamber described by Blom¹⁶ may be used for a fairly accurate estimation of the concentration of spermatozoa by comparing the concentration of spermatozoa in a layer of semen 50 microns thick with pictures of known concentrations of 1, 0.5 and 0.2 million spermatozoa per cmm.

5. Other methods not so practical as the above for determining the concentration of spermatozoa include the measuring the packed cell volume, spermatocrit,⁴¹ and the use of the Coulter electronic counter.⁴⁸

Motility of spermatozoa at the time of collection is

commonly used and excellent measure of the fertilizing ability of spermatozoa. Care should be taken at the time of collection that the ejaculate is protected from "cold shock" or sudden reduction in temperature that has a marked depressing effect on motility. Excessive heat and chemicals or foreign agents, as well as urine or water, also affect sperm cells and reduce motility. The first ejaculate after a long period of sexual inactivity often has poor motility and increased numbers of dead spermatozoa.

For accurate results this test is best made with an electrically heated microscope stage at body temperature. Motility ratings can be made in the field by gently warming the semen slide by placing it on a flat bottle containing warm water at body temperature. Cooling semen from body temperature down to refrigerator temperature causes a gradual loss of motility of spermatozoa until near immobility is reached. Therefore, semen should always be examined at body temperature so that accurate and comparative readings can be made. It may be desirable to dilute the semen in warm Ringer's saline or 2.9 percent sodium citrate solution to more easily observe the individual spermatozoa so an estimate of the degree and percentage of motile spermatozoa can be made. A fast, accurate, photographic method of measuring the proportion of moving spermatozoa and their rate of progression has been described.⁷⁹ Motility of bovine spermatozoa is more significant as a test for fertility after thawing following freezing. A motility rate less than 20 percent after thawing will contribute to a low non-return rate.^{77a} A time-exposure photographic system with dark-field microscopy has proven a valuable procedure to determine spermatozoan motility and semen quality following thawing of frozen bull semen.^{77b} By this technique the number of progressively motile cells, which varies widely between ejaculates and bulls, can be assessed with great accuracy.

Motility is based on the estimated percentage of motile spermatozoa and their degree of motility. Most investigators described the various degrees of motility of spermatozoa in undiluted semen as follows:^{53,55}

- 0—spermatozoa are immotile
- 1—stationary bunting or weak rotary movements are exhibited by spermatozoa
- 2—oscillatory or rotary movements and fewer than 50 percent of the spermatozoa are in progressive motion, with no waves or eddies
- 3—progressive rapid movement of spermatozoa, with slowly moving waves and eddies, usually 50 to 80 percent of the spermatozoa must be progressively motile to produce waves and eddies
- 4—vigorous, progressive movement with rapid and

abruptly forming waves and eddies, indicating about 90 percent motile spermatozoa

5—very vigorous forward motion, extremely rapid waves and eddies, indicating about 100 percent actively motile spermatozoa

In the 350 micron thickness of undiluted semen in a comparing chamber at body temperature, 50 to 70 percent living spermatozoa produced rapid whirls and eddies and good to excellent motility; 30 to 50 percent produced sluggish waves and fair motility; and 10 to 30 percent motile spermatozoa produced single propulsions with no waves or whirls and with poor motility.¹⁶ In normal bovine semen initial motility of 40 to 45 percent or more was essential since lower rates of motility were associated with infertility. Most fertile bulls have 50 to 80 percent of their spermatozoa exhibiting active, progressive motility.^{16,20}

Good initial motility alone is not always an accurate indication of fertility in the bull.¹¹⁴ Examples of infertile bull semen with excellent initial spermatozoan motility that rapidly lost its motility when stored or highly motile spermatozoa that were infertile were cited. No difference was reported in conception rates of semen with 50 percent actively motile spermatozoa and higher percentages of motile sperm cells. Motility below 50 percent was often associated with lower conception rates or poor fertility.

The motility of bovine spermatozoa in testicular hypoplasia was much poorer than in testicular degeneration.⁵³ Only 10 percent of the bulls with testicular degeneration showed motility above 70 percent and a rate or degree of motility of 3 or higher, which is the average requirement. The number of motile spermatozoa was less than 70 percent in 90 percent of the bulls with testicular degeneration but the degree of motility was below 3 in only 42 percent. Ninety-two percent of 100 normal fertile bulls had satisfactory motility whereas only 32 percent of the "problem" bulls had satisfactory motility.^{16,20} Congenitally sterile bulls with a very high percentage of abnormal sperm cells, especially those with defects of the midpiece and tail, had the lowest motility.^{53,99} It is generally assumed that the duration of motility of abnormal spermatozoa is reduced.

Normal stallion spermatozoa had a degree of motility of 3 to 4, and 48 to 75 percent of the spermatozoa in the semen were actively motile about 20 minutes after ejaculation.⁸³ After the unextended semen had stood 8 hours at room temperature no reasonable degree of activity was observed.⁸³ The percentage of motile spermatozoa in 54 fertile stallions ranged from 55 to 60 percent.^{12,13} In several thousand stallions examined low motility or as-

thenospermia occurred in 0.8 to 3.4 percent and necrospermia occurred in 0.09 to 0.3 percent. Even with the minimum of handling, the motility of equine spermatozoa decreased rapidly in vitro.⁸³ This is a possible reflection of the inability of equine spermatozoa to survive in equine seminal plasma that has very low levels of reducible sugar for energy purposes in contrast to the relatively long viability of spermatozoa in seminal plasma of other animals. The addition of isotonic, 5 percent, glucose to equine semen with poor motility of the spermatozoa, may result in marked improvement of the motility.⁹⁶ This is interesting, since in the genital tract of the mare equine spermatozoa survived 72 hours or more.³⁵ (See equine reproductive physiology) In horses it is possible that seminal plasma may have an adverse effect on spermatozoa while the environment of the mare's genital tract is highly favorable for sperm cell survival. Thus some stallions with relatively poor motility in freshly ejaculated sperm may be quite fertile. Even so, in the stallion the spermatozoan motility and the quality of that motility are the most reliable estimates of fertility.¹¹⁸

In rams,⁵⁰ boars⁵⁸ and bulls a decreased motility of spermatozoa has been reported in experimentally-produced testicular degeneration. Fertile boars have semen that usually contain 80 to 95 percent actively motile spermatozoa, while rams have about 60 to 70 percent motile cells. In man 50 to 60 percent active spermatozoan motility was average and 75 percent was good.^{81,82} In men with less than 40 percent actively motile spermatozoa the incidence of sterility rose sharply.

Sperm cell defects involving the midpiece and tail are often characterized by poor motility. There is an intimate relationship between the epididymis and its secretions on sperm cell motility and tail defects as described under diseases of the epididymis.

Pus and drops of vaseline in the semen reduced spermatozoan motility.^{10,16,20} Care should be used in lubricating an artificial vagina not to apply an excess of lubricant that might melt and run into the semen-collecting tube or vial.

The importance of the number of actively motile sperm cells in the ejaculate on the fertility of the male has been stressed in different species by many workers. This fact was well-illustrated by a valuable, 12-year-old Guernsey bull used in an artificial insemination stud that developed senile testicular degeneration associated with interstitial cell tumors. A progressive gradual decline occurred in motile spermatozoa in the ejaculate from 50 to 10 percent along with a gradual increase from 30 to 60 percent in the number of abnormal spermatozoa. Extending his semen on the basis of the numbers of actively motile

spermatozoa present in each ejaculate resulted in satisfactory conception rates even though the extension rates were as low as 1 to 10 in order to provide 6 to 10 million actively motile spermatozoa per ml. for each insemination.

Longevity, viability, or liveability of spermatozoa in semen or extended semen at refrigerator, room or incubator temperatures is another measure that can be used for testing or estimating the fertility of semen. A number of studies from 1940 to 1955 were summarized in the first edition of this text and others of work performed on this type of test for assessing semen quality and fertility.^{7,98} Since that time relatively few experimental studies on these tests have been conducted because they are difficult to run as they extend over a period of hours or days, and thus are not adaptable to semen collected for artificial insemination purposes. Good quality equine semen maintained reasonably good motility for up to 8 hours after collection at room temperature.⁸⁵ Results and correlations with fertility of the male do not provide any greater predictive value than the current simpler tests of semen quality including concentration, motility, and morphology.

Differential staining to determine live/dead spermatozoa in an ejaculate was described using a vital stain such as eosin nigrosin stain.^{18,20,115} This stain, as the India ink, is a good background stain. To make the staining solution, weigh out 3 gms. of sodium citrate dihydrate and add to 100 ml. of sterile double distilled water. To this add 1 gm. eosin B and 5 gm. nigrosin and mix into solution. The eosin will stain the dead spermatozoa a pink or red color, live spermatozoa remain colorless, and nigrosin provides a blue-black background stain.¹⁸ This stain will remain stable for one year or more without refrigeration. Place a small drop of stain on a clean warm slide and add a small drop of semen to the stain and mix gently with a round glass rod or a platinum loop. After a few seconds to a minute or more smear out with the glass rod or another glass slide and dry rapidly near a flame. At least 100 to 200 cells, or preferably 500, should be counted by scanning the entire length of the semen smear. Morphologically abnormal cells may be counted at the same time. In a review on the assessment of semen quality, most workers found an average of about 20 percent dead cells in most normal bovine semen samples and there was little correlation with fertility.² After a prolonged period of sexual rest the percentage of dead spermatozoa may be increased. The live/dead sperm cell count should be evaluated critically. Poor stain or staining technique may greatly affect the findings. A high incidence of necropermia is usually associated with poor

motility and low fertility. However, poor motility may be associated with normal levels of live spermatozoa, which depending on the cause of the poor motility, may be characterized by either normal or low fertility. Presently the live-dead spermatozoan ratio in ejaculates is seldom used to assess fertility.

Examination of stained spermatozoa for morphology is of definite value in studying the severity of testicular degeneration or testicular hypoplasia and the congenital or hereditary defects of spermatozoa.

Techniques for preparing and staining sperm cells for morphology examination—The importance of making smears, and fixing them by air-drying before the semen is cooled to prevent the development of secondary spermatozoan abnormalities has been emphasized.⁹⁷ Storing semen a reasonable time had no effect on the primary spermatozoan abnormalities. Extended semen is not satisfactory for morphological examination because of the egg yolk or milk that is present. Semen samples could be diluted with a physiological saline solution to a concentration of about 200,000 per cmm. before a slide is prepared, so that the stained spermatozoa will not be too concentrated to permit observation of individual cells.¹⁸⁻²⁰ All glass slides used in making semen smears should be thoroughly cleaned, soaked in alcohol, and dried. The plasma and gel fraction of semen may interfere or make difficult the staining of equine or porcine spermatozoa. The addition of one-half to one part of five percent of isotonic glucose solution to one part of horse semen was recommended.⁹⁶ This mixture was centrifuged at 1500 rpm in a clinical centrifuge for 5 minutes. After pouring off the plasma the sperm cells in the glucose solution are stained in the usual manner.

India ink preparations, are probably the simplest and easiest for the veterinary practitioner to prepare.^{19,20} Five parts or drops of a high-grade India ink, such as Pelican Yellow Label, are gently mixed with 1 part or drop of semen. One should be careful not to contaminate the bottle of India ink with sperm cells or bacteria. A drop of this mixture is placed on the slide and spread by one of the following methods: blowing gently; drawing, not pushing, it out with a spreader as with a blood smear; or gently smearing it out with a 1/8 inch, rounded, glass rod. The smear is then air-dried or dried slowly over the warm air of a flame. The dried slide is examined under oil immersion or the high dry magnification. All abnormalities of the spermatozoa and semen may be noted. Large round cells, if present, should be recognized as leukocytes or primordial germinal cells.

Eosin-nigrosin stain is a widely-used simple and effective vital stain.^{18,115} The technique for its use was de-

scribed previously. It may be used for counting the numbers of live/dead cells as well as the morphologically normal and abnormal cells.

Wright's stain, commonly used for staining blood smears, may also be used for semen examinations. This stain is not as satisfactory as **Casarett's stain** because it tends to precipitate on the slide, producing artifacts, and it does not stain the spermatozoa as effectively. The semen should be smeared gently and thinly over a clean slide and fixed by air-drying. The slide should then be immersed in 0.5 or 1 percent chloramine T solution to remove the excess mucus, even though this procedure may cause some breakage of spermatozoa. After being immersed in this chlorine solution for 5 to 7 minutes, the film of semen on the slide is washed gently first with distilled water and then with 95 percent alcohol, and then dried. The semen film on the slide is covered with Wright's stain for 60 seconds. Distilled water is then added until a metallic luster is produced. The stain is left on the slide for 2 to 5 minutes before being rinsed off with distilled water. After the stained slide is air-dried it can be examined under the oil immersion or the high dry power of the microscope. **Hematoxylin and eosin and Giemsa's stains** are also satisfactory for the examination of semen smears for the presence of cells other than spermatozoa.

Casarett's stain is an excellent stain for semen slides.¹⁰ Thin films of fresh semen are fixed on glass slides by immersing them for 3 minutes in a mixture of equal parts of ethyl alcohol and ether; the slides are then air-dried. They are stained by immersion for 5 to 7 minutes in a dye solution heated to 40 to 60° C. The dye solution consists of 30 ml., or 2 volumes, of 5 percent watery eosin B. solution and 15 ml., or 1 volume, of 1 percent watery phenol solution. The stained smears are washed with distilled water, air-dried, and mounted in balsam. The spermatozoan structures are very clearly outlined. Other good staining techniques have been described including **carbofuchsin and eosin stain** and **methylene blue**.⁴

For long term preservation of spermatozoa, especially for acrosomal examination, adding a few drops of semen to a small amount of buffered formo-saline made up and used as follows is recommended:^{47,51,52}

Stock buffer soln*	100 ml.
Stock NaCl soln.**	150 ml.
Commercial formalin (37-40% formaldehyde)	62.5 ml.
Aq. dist. ad.	500 ml.
*Stock buffer soln.	
soln. A) $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$	21.682 gm.
Aq. dist. ad	500 ml.
soln. B) KH_2PO_4	22.254 gm.

Aq. dist. ad. 500 ml.
Take 200 ml. of soln. A and mix with 80 ml. of soln. B. Then from the resultant 280 ml., take 100 ml. as stock buffer soln.

**Stock NaCl soln.

NaCl 9.01 gm.
Aq. dist. ad. 500 ml.

Directions for use:

Add 1 to 2 drops semen to about 5 to 10 ml. of buffered formo-saline, gently shake; add 1 to 2 drops of dihydrostreptomycin, incubate for 10 to 20 min. at 37° C and then refrigerate (about +4° C); this will preserve sperm cells for up to 18 months. Another method for fixing bull or boar spermatozoa for shipping or storing was to use glutaraldehyde in phosphate buffered saline with sodium cacodylate.^{65,68}

Wet mounts for phase contrast microscopy are made in a suitably equipped laboratory from preserved samples and are far superior to smeared and stained preparations for estimating the percentage of spermatozoa with proximal protoplasmic droplets and acrosomal abnormalities. A phase contrast effect can be partially achieved in a regular light microscope by reducing the amount of light permitted to come through the substage condenser. Following one or more of the several staining procedures 100 to 200 or more up to 500 to 1000 spermatozoa should be examined under oil immersion at 1,200 magnification and classified.

An experienced technician could achieve as reliable results counting 100 cells as by counting 500 sperm cells.¹⁰⁷ Spermatozoan abnormalities may be classified as head, body, and tail defects. These three anatomical groups of sperm cell abnormalities have been classified by Lagerlof and Blom^{19,20,47} in two further groups as primary forms that occur due to disorders of the seminiferous or germinal epithelium and as secondary forms that occur after they have left the germinal epithelium, during their passage through the mesonephric ducts, during ejaculation, or in manipulations of the ejaculate including excessive agitation, over-heating, too rapid cooling, due to the presence of water, urine or antiseptics in the semen, and etc. The primary anomalies occur during spermatogenesis either during spermatocytogenesis from spermatogonia to spermatids or during spermiogenesis from spermatids to spermatozoa.

The author and others^{46,47} have serious reservations over using these latter two classifications of spermatozoan abnormalities. If a sperm cell is defective and for that reason can't fertilize an ovum it doesn't matter whether it becomes defective in the seminiferous tubules or mesonephric duct or at ejaculation. If sperm cell artifacts are due to accidents from improper handling of the ejac-

ulate or smearing or staining, a subsequent ejaculate, if handled properly, will usually lack such damaged cells. Furthermore, defects occurring in the germinal epithelium may not manifest themselves until later in the maturation of the cell such as separation of the head and neck described in Guernsey bulls^{51,52} in which the separation took place in the head of the epididymis at the time of the loosening of the cytoplasmic or protoplasmic droplet which up to this point had apparently prevented the separation.

Chromosomal defects in apparently normal sperm cells have been discussed previously and are probably genetic in nature. (See prior discussion in this Chapter on abnormal acrosomes, nuclear defects, intrachromosomal aberrations in spermatozoan development and hereditary or congenital sperm cell defects.)

Spermatozoan head abnormalities include: (See Figures 198, 199, 200)

- Microcephalic heads
- Macrocephalic heads
- Double, or multiple heads
- Elongated or narrow heads
- Pyriform or pear-shaped heads with a narrow or tapering base
- Twisted, irregular-shaped heads and abortive forms
- Round short heads

Abnormal acrosomes (Knobbed spermatozoa) "ruffled," incomplete, flattened, or "bent-over" acrosomes

Nuclear envelope invaginations "craters," "pouches," "erosions" (near equator)

Detached or free heads (Guernseys and others)

Detached galea capitis and acrosome

The latter two are possible "secondary" abnormalities. Macrocephalic heads with a broader than normal base have been shown by various tests to probably be cells with a diploid chromosome content. These were found with an incidence of 0.104% in a group of inbred or closely line-bred Hereford bulls¹⁰⁴ and as a rare occurrence in six bulls with lowered fertility.⁴⁶ Abnormal acrosomes and nuclear abnormalities may be difficult to observe or detect without phase contract microscopy, electron microscopy, or special staining procedures. A review has been compiled on recent studies on acrosomal changes associated with aging of spermatozoa and in freeze-thawed spermatozoa as another indicator of sperm quality since penetration of the ovum depends on acrosomal enzymes.^{26,101} Detached or free heads may be due to excessive agitation of the semen sample or due to improper smearing of the spermatozoa on the slides. The detached galea capitis or head cap from dead spermatozoa is seen mainly in India Ink preparations in the

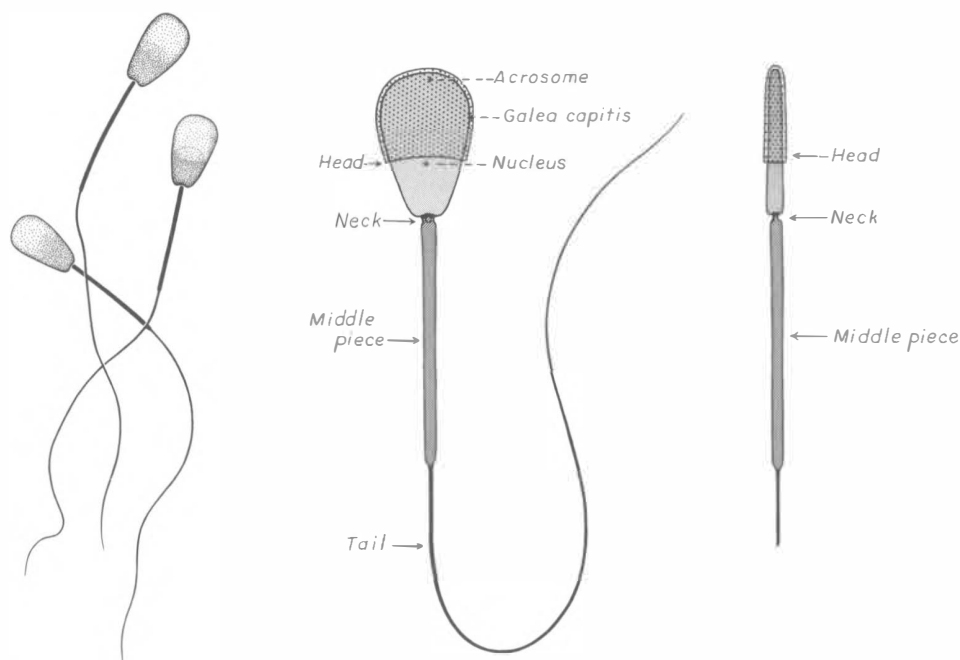


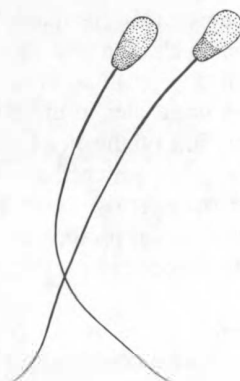
Figure 198. Normal Bovine Spermatozoa (Left) Normal Spermatozoa, (Center) Diagram of Dorsoventral Aspect, (Right) Diagram of Lateral Aspect.



Normal Sperm Cells



Microcephalic Sperm Cells



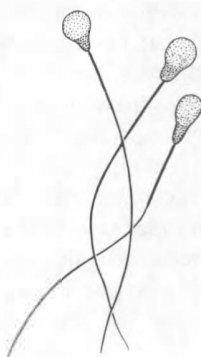
Macrocephalic Sperm Cells



Short Broad Heads



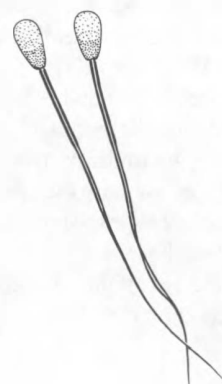
Elongated Narrow Heads



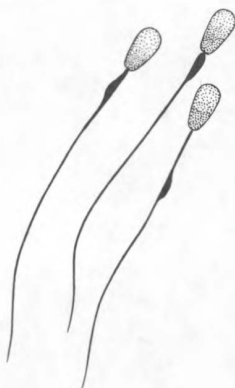
Pyriform or Pear-Shaped Heads



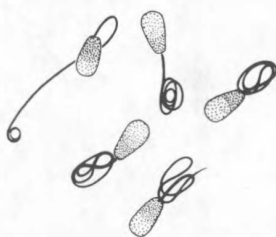
Double Heads



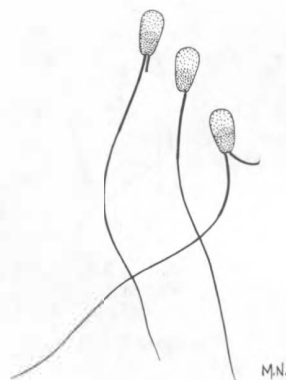
Double Middle Pieces and Tails



Swelling of Middle Pieces



Kinked and Coiled Middle Pieces and Tails



Abaxial Attachments of Middle Pieces (may be normal in stallions and boars)

Figure 199. "Primary" Spermatozoan Abnormalities.

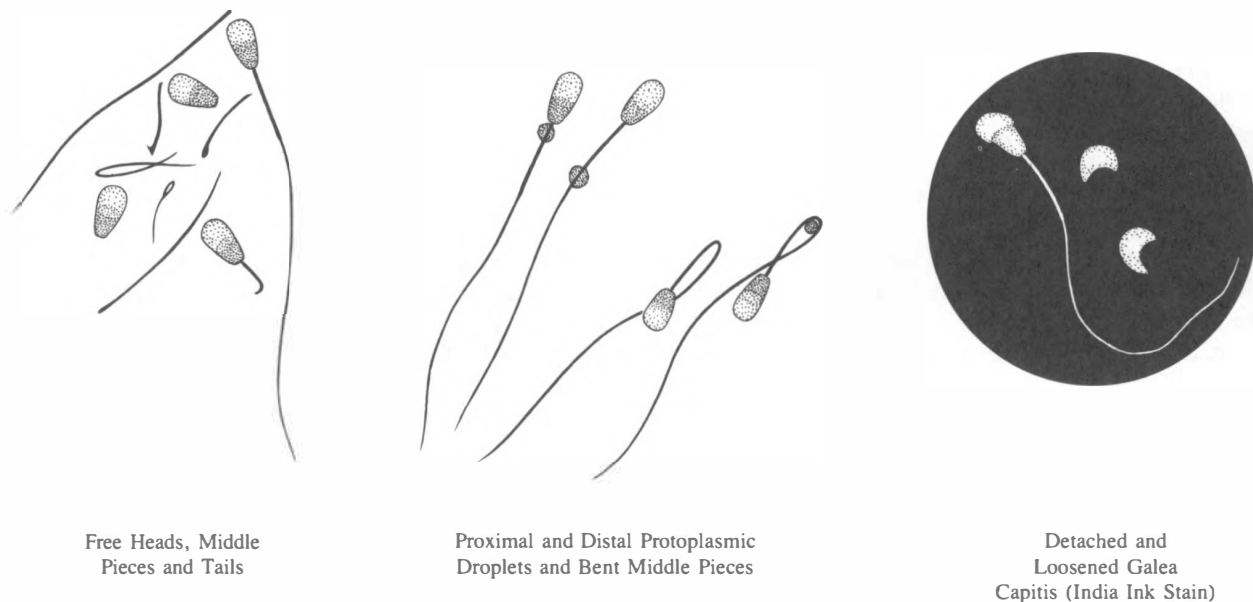


Figure 200. "Secondary" Spermatozoan Abnormalities.

first ejaculate after a long period of sexual rest or in spermatozoa after prolonged storage. They resemble a bathing cap in shape. Using a special stain, less than 5 percent of acrosomal abnormalities in sperm cells from bulls being collected regularly but an average of 21 percent abnormalities of the acrosome in the first ejaculates of 22 sexually-rested bulls was found.¹¹⁹ This may be an aging phenomena.^{101,106}

An increased number of tailless heads occurred in the early stages of testicular degeneration in fertile bulls.^{19,20,53,99} Normal fertile bovine semen contained only 0.5 to 8.6 percent loose heads. The stallion and possibly the boar spermatozoan differs from other mammals by having an asymmetric head, an abaxial position of the tail and a small acrosome.^{14,15,64b,65,66}

Spermatozoan body or middle piece abnormalities include: (See Figures 199 and 200)

- Swollen neck
- Kinked neck with coiling of the middle piece and tail about head
- Stubby midpiece ("tail stump" defect)
- Naked or filiform neck
- Abaxial attachment of the neck and middle piece to the head, (normal in stallion and boar^{15,64b})
- Swelling of the middle piece, either diffuse, localized, cranial or caudal
- Double middle piece
- Coiled middle piece
- Kinked middle piece with a tightly coiled tail

"Corkscrew" middle piece

Loose or free middle-pieces and tails; these may be weakly motile

Kinked necks

Middle pieces with proximal or distal protoplasmic or cytoplasmic droplets

Bent middle pieces, with or without a protoplasmic droplet at the point of the greatest bending

In counting abnormal sperm cells, loose or free middle pieces and tails should not be recorded if free heads are counted. The presence of a protoplasmic or cytoplasmic droplet on the middle piece has been described^{19,20,74,97} and is considered to be normally present on spermatozoa from the head of the epididymis. As the spermatozoa mature in their passage through the epididymis this protoplasmic drop recedes from the neck down the middle piece and is usually lost before the spermatozoa are ejaculated. The migration of the propoplasmic droplet from the proximal to the distal portion of the middle piece occurred in the head of the epididymis. These were considered to be immature sperm cells when seen in ejaculated semen.⁷⁴ No more than 2 to 3 percent of normal spermatozoa should have this protoplasmic drop on the proximal part of the middle piece.^{16,20,74} Other authors indicated that the presence of a high percentage of middle pieces with protoplasmic droplets may possibly be due to overuse of the male and to too rapid passage of spermatozoa through the epididymis. In boars this condition was associated with testicular degeneration and

hypoplasia.⁵⁸ A localized swelling of the middle piece should be differentiated from an attached protoplasmic or cytoplasmic droplet. The true developmental abnormality of a swelling of the middle piece is an irregular enlargement which stains darkly, in which no differentiation can be seen between the swelling and the central fibril; and the ends of the swelling are tapered.⁹⁹ The protoplasmic droplet, by contrast, stains less intensely and is quite spherical. The corkscrew and "stubby" middle piece are unusual abnormalities.^{21,22b,32b} Abnormalities of the middle piece and tail interfere with fertility by reducing motility; the swollen and thickened types of midpiece abnormalities were most serious.^{53,99} A constant content of 30 to 50 percent of bent middle pieces was usually associated with impaired fertility.⁴ An abnormal environment in the epididymis may result in midpiece or tail defects. An abaxial location of the midpiece on the head of the spermatozoa is common in stallions and possibly boars and is not associated with infertility in those species.^{14,15,65,66} An incidence of 35 to 47 percent abaxial midpieces in stallions was reported.¹³

Spermatozoan tail abnormalities include: (See Figures 199 and 200)

Tightly coiled tails (Dag defect)

Double tails

Distal cytoplasmic or protoplasmic droplets (common in boar semen)

Absent or shortened tails, seen most often in stallions

Coiled tails

Bent, "hairpin" tails, with or without a protoplasmic drop at the bend

Broken tails

The latter two conditions^{66,72} are possible "secondary"

abnormalities in boars associated with infrequent use rather than overuse. Proximal protoplasmic or cytoplasmic droplets on the body or midpiece if present on a high percentage of cells is usually associated with infertility, especially in boars. Distal protoplasmic droplets are common, about 10 to 12 percent, in boar semen and are not associated with infertility.^{64b} In general abnormalities of the tail are infrequent and of little importance. Tails bent at the junction of the tail and middlepiece; either with or without a protoplasmic droplet, are fairly common. They are usually caused by cold shock or osmotic shock due to the presence of water or urine in the ejaculate.

The presence of 10 percent or more of any single type of the above head, body or tail abnormalities, normally absent from semen of males, is often associated with reduced fertility.⁵²

Cells other than spermatozoa in semen smears include:

Leucocytes are found in cases of inflammation or infection of the reproductive tract; there are very few in normal semen

Erythrocytes

Squamous epithelial cells—both nucleated and non-nucleated. These usually come from the epithelium of the prepuce or the urogenital ducts.

Boat-shaped spermatogenic cells—These are more common in abnormal than in normal semen and are more likely to be associated with deformed heads than with deformed middle pieces.^{53,99}

Spermatids—nucleated, non-nucleated, and multi-nucleated.

Spermatocytes—primary and secondary, often called

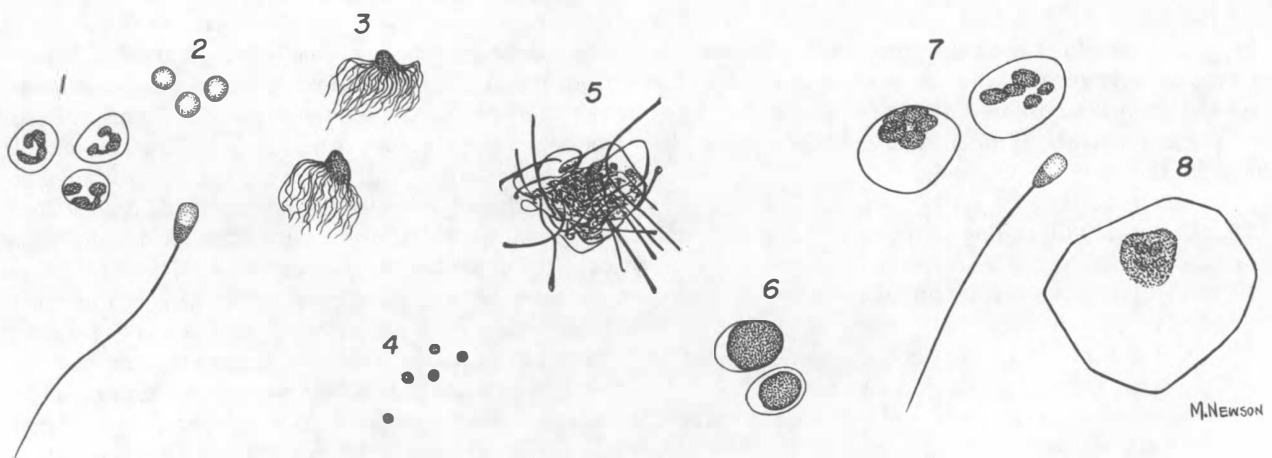


Figure 201. Miscellaneous Cells Found in Semen 1. Leukocytes 2. Erythrocytes 3. Medusa Formations 4. Protoplasmic Droplets 5. Degenerating Sperm Cell Cluster 6. Primordial Spermiogenic Cells 7. Giant or Multinucleated Cells 8. Squamous Epithelial Cells.



Figure 202. Normal Bovine Spermatozoa

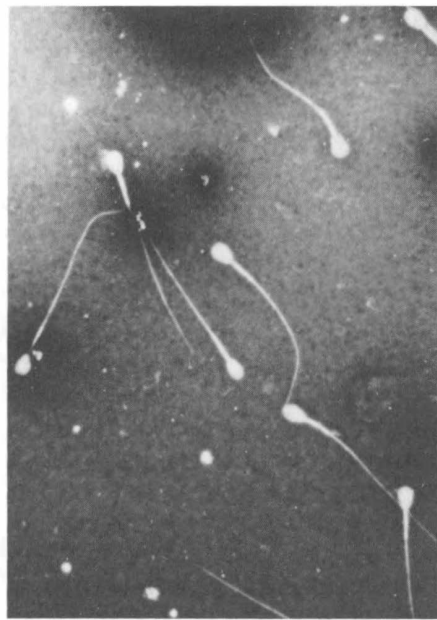


Figure 203. Normal Canine Spermatozoa (India Ink Stain) (Courtesy K. McEntee).

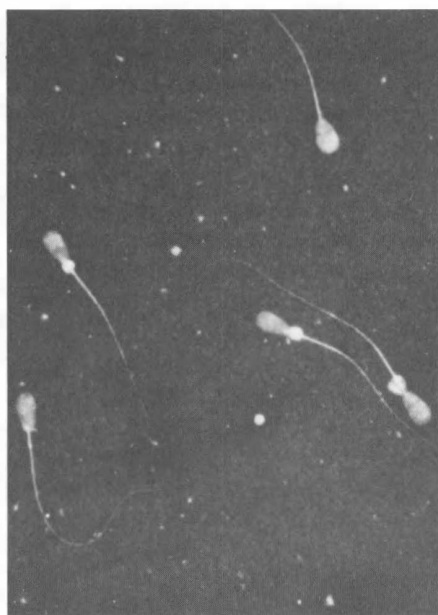


Figure 204. Proximal Protoplasmic Droplets on Bull Spermatozoa (India Ink Stain) (Courtesy K. McEntee).

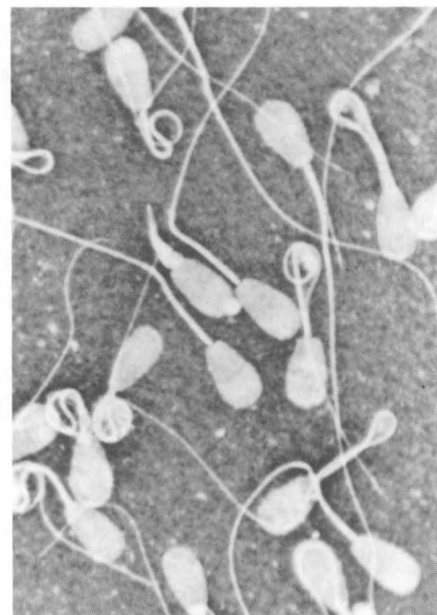


Figure 205. Coiled Tails and Middle Pieces in an Infertile 11-year-old Bull. (The motility rate was between 5 and 10 percent, yet the conception rate was 50 percent with liquid semen extended 1:10 to 20.)

"spheroids" or primordial spermatogenic cells.

Medusa cells or bodies—Medusa formations are portions of ciliated epithelial cells from the efferent ducts of the testis.¹⁷ They are deeply-staining cells about the size of the head of the spermatozoa, with 10 to 30 filiform, or long brush-like, projections or cilia. These cells are seen only in rare instances in the usual sperm cell preparations but may be seen in much greater number in semen preparations from males with severe testicular hypoplasia when the semen is centrifuged and the sediment is placed on a slide and stained. This finding may aid in differentiating between an incomplete ejaculation of a normal bull and a complete ejaculation of a bull with nearly completely suppressed spermatogenesis. These medusa formations are seen at a rate of about 1 to 10,000 spermatozoa in normal bulls. In stallions the incidence is higher.

Protoplasmic or cytoplasmic droplets; floating free in semen, are often observed in fertile semen and are of no significance.

Bacteria, molds, and protozoa are usually contaminants from the prepuce.

Degenerating spermatozoan clusters—were observed in 19 percent of fertile bulls and 79 percent of bulls with testicular degeneration.⁵³ Occasionally they were seen in bulls with testicular hypoplasia. These clusters of spermatozoa are apparently produced by a disturbance in spermatogenesis.

Multinucleated giant cells with 6 to 8 nuclei are seen occasionally in males with testicular hypoplasia or degeneration and are due to abnormalities in the divisional mechanism of the primary spermatocytes.³³ The cause of these latter two conditions might be similar.

The determination of the number and type of abnormal sperm cells in an ejaculate should be used along with other examinations conducted immediately after collection such as those for motility and concentration. There is a divergence in opinion as to the importance of the presence of varying numbers of abnormal spermatozoa seen on stained semen preparations. If the percentage of abnormal spermatozoa is not above 30 to 35 percent it is not correlated with fertility in the relatively fertile bulls.^{25,114} An average of 31.4 percent abnormal spermatozoa was reported with a range of 15 to 48 percent in 19 bulls with testicular degeneration⁵³ and an average of 39.1 percent abnormal spermatozoa with a range of 22 to 58 percent in 4 bulls with testicular hypoplasia. Normal fertile bulls had an average of 15.1 percent abnormal spermatozoa with a range of 6 to 26 percent. The semen of normal fertile bulls should not have more than 3 to 4 percent abnormal heads, 4 to 10 percent abnormal middle pieces, 0.5 to 2 percent abnormal tails, and 0.5

to 6 percent, tailless heads.^{53,99} Similar values of 1.2 to 10.4 percent, with an average of 4.6 percent, primary spermatozoan abnormalities and an average of 2.1 percent, with a maximum of 8.6 percent, loose heads and other secondary abnormalities were reported in normal fertile bulls.^{19,20}

Rams and bucks have very similar semen characteristics including, volume, concentration and motility parameters.^{87,91} Rams having more than 14 percent abnormal spermatozoa in their semen are probably of reduced fertility providing the ejaculate was not taken after a long period of sexual rest.⁸⁷ Normal fertile ram semen should not contain more than 5 to 15 percent abnormal spermatozoa.¹¹⁷ Rams having 0.1 percent abnormal spermatozoa in their semen had an approximate fertility of 80 to 100 percent; those with 1 percent abnormal spermatozoa had fertility rates of 60 percent; rams with 10 percent abnormal spermatozoa had fertility rates of 45 percent; those with 30 percent abnormal spermatozoa had a fertility rate of 20 percent; and rams with more than 50 percent abnormal spermatozoa were sterile.⁵⁰

Less than 14 to 17 percent with a range of 6 to 10 percent abnormal spermatozoa was observed in the semen of fertile boars.^{58,92} In 13 boars with testicular degeneration the abnormal spermatozoa varied from 3 to 36 percent and immature spermatozoa with proximal protoplasmic droplets from 1 to 95 percent. The number of abnormal sperm cell heads was over 20 percent in 5 of the 13 boars and in 5 others the percentage varied from 3 to 8. The numbers of immature spermatozoa with proximal droplets were high in most cases of porcine testicular degeneration.⁵³ Conception rates were 67.7 percent, 57.3 percent and 45.5 percent with boars with 80 to 100 percent, 60 to 79 percent and 40 to 59 percent normal spermatozoa, respectively, including sperm cells with distal protoplasmic droplets.¹⁴ The number of cells with distal and even proximal protoplasmic droplets were extremely variable between boars and between ejaculates. Tightly coiled tails appeared to be a defect in spermatogenesis and doubling of a portion of the cells occurred at a level of 0.3 percent. A majority of midpiece attachments were slightly abaxial in the boar and this defect should not be considered as a primary sperm cell defect in the boar as it is in the bull.¹⁴

Many workers have reported that it was more difficult to evaluate the spermatozoa of stallions than of bulls, rams, boars and dogs.^{12-14,71,74,83,100} In the Thoroughbred stallion infertility can exist in the presence of apparently normal semen quality and it was concluded that the actual fertility of a stallion cannot always be predicted on the basis of a semen examination.^{83,100} Other authors^{35,12-14} reported on sterile stallions with semen

containing only dead spermatozoa (necrospermia) at the time of ejaculation. In stallions of low fertility the concentrations of spermatozoa and the volume of semen were low, 10,000 to 15,000 per cmm. and about 10 to 25 ml., respectively. A fertile stallion was described with good sperm motility but with 35 to 45 percent of the spermatozoa having a proximal protoplasmic droplet and 4 to 6 percent having double heads.³⁵ Bielanski^{12,13} reported on 54 stallions with conception rates from less than 25 percent to nearly 100 percent and the primary spermatozoan abnormalities varied from 2.5 to 10 percent and the secondary abnormalities from 22 to 39 percent. The most fertile stallions had less than 3 percent primary abnormalities. The author observed a young Standardbred stallion with 60 to 70 percent grossly abnormal middle pieces and associated poor motility. Under regular handling infertility was evident but by good management, controlled breeding and breeding at the proper time of estrus he achieved a 70 percent conception rate the next four years. In general the presence of more than 20 percent abnormal spermatozoa in equine semen may be interpreted as indicating low fertility but there were many exceptions.³⁷ Some stallions may have apparently normal spermatozoa and low fertility; others are highly fertile even though a rather high percentage of spermatozoa are abnormal. Five to 13 percent abnormal spermatozoa in semen of fertile stallions was reported.⁸⁶ Up to 30 percent abnormal spermatozoa may be present in fertile equine semen.¹¹

Less than 20 percent abnormal spermatozoa were present in dogs producing good quality, fertile sperm.^{54a,69,90a} Only 0 to 10 percent abnormal spermatozoa with an average of 4.8 percent in fertile canine semen was reported in another study.^{52b} Ten to 15 percent abnormal sperm cells were reported by other authors in 11 normal dogs.^{5,24} Four to 10 percent abnormal spermatozoa were reported in ejaculates of 6 fertile male cats.^{111,a,b} The most common abnormalities were cytoplasmic droplets, double, bent, dubbed or shortened tails and enlarged middle pieces.

It is obvious from the above discussion that great care must be used in the interpretation of the morphology of spermatozoa in semen samples. Technicians differ in their classification of sperm cells, some classifying certain cells as abnormal that others would classify as normal. Differences arise due to variations in the technique of handling and preparing slides. There is probably no distinct line of demarcation between animals of good and poor fertility. The morphological examination of semen as an aid in evaluating fertility is apparently of greatest value in the detection of males whose fertility is unsatisfactory in natural matings. It is of limited or questionable value

in determining fertility in individual ejaculates from males of fair to good fertility used in artificial insemination.

The revised criteria (1976) of the American Society of Theriogenology¹¹⁰ for the evaluation of the breeding soundness (BSE) in bulls is scored or based on three reliable characteristics that have been correlated to fertility. These are:

- | | |
|---|------------------|
| 1. scrotal circumference (based on the age of the bull) | 10 to 40 |
| 2. percent abnormal spermatozoa (primary and total) | 3 to 40 |
| 3. motility (gross and individual) | 3 to 20 |
| Total score | 16 to 100 |

Bulls receiving scores from 60 to 100 are graded as satisfactory, 30 to 60 as questionable and below 30 as poor potential breeders. This presumes that the bull is normal physically, has satisfactory libido and is managed properly. In a Nebraska breeding trial with 57 satisfactory bulls, 22 questionable and 22 poor potential breeders, the conception rates were 60, 48 and 30 percent, respectively.¹¹⁰

The current, revised (1976) values for these three criteria are as follows:

Scrotal circumference (given previously in this Chapter, page 860)

Classification	Percent Abnormal Spermatozoa		
	Primary (%)	Total (%)	Score
Very good	10	25	40
Good	10-19	26-39	25
Fair	20-29	40-59	10
Poor	29	59	3

Classification	Motility (Vigor of Movement) of Spermatozoa		
	Gross	Individual*	Score
Very good	rapid swirls	rapid, linear	20
Good	slower swirls	moderately fast, linear	12
Fair	shaky	slow, linear	10
Poor	flickers	very slow, erratic	3

*Must evaluate in a compatible diluent

Although these current criteria and tests used for the evaluation of the breeding soundness of bulls have been simplified and made more repeatable, it is probably advisable to continue the "battery" of semen tests, particularly on certain bulls to identify those with unusual semen characteristics.

Bacteriological or virological examination of semen

may be indicated under certain circumstances, especially when evidence of genital inflammation or infection is present in females following breeding to a male, a rapid decline in motility of the spermatozoa occurs on storage, or an increase in pH or the presence of leukocytes or frank pus are present in the ejaculate or in the semen smear. Organisms or viral agents in the semen may come from the testes or epididymides, the accessory glands, the vas deferens, the urethra, or the prepuce or penis. Semen examination of bulls by cultural methods or by the injection of semen into test animals may reveal infection with brucellosis, trichomoniasis, vibriosis, mycoplasmosis and others. In cattle the fluorescent antibody test has proven useful in the examination of preputial smegma samples for vibriosis. In brucellosis, semen plasma agglutination tests may be indicated if the blood test reveals a positive or suspicious titer. Besides the possible danger to the female by introducing infection at the time of coitus, bacteria and their products may injure the spermatozoa and result in a rapid decline in the motility of stored sperm cells, especially in liquid or frozen extended semen. (See prior discussion in this Chapter on genital infections of the male.)

A brief summarization of the infectious organisms, either venereal, systemic, or "opportunistic" found in the semen of bulls include: diptheroids, **C. renale**, streptococci, **B. pyocyaneus**, *Leptospira* spp., staphylococci, **E. coli**, **C. pyogenes**, **Br. abortus**, *Mycobacterium tuberculosis* (bovine and avian types) *Mycobacterium paratuberculosis*,⁷⁵ **Ps. aeruginosa**, actinomycetes, *Proteus*, micrococci, yeasts, bacilli and molds. *Mycoplasma* were found in 94 percent of the semen samples from bulls.² This organism was a saprophyte in the prepuce of nearly all bulls. *Mycoplasma* were readily recovered from the sheaths of 80 percent of 160 bulls, and less commonly from the semen.^{1a,67a,90b} Which of these mycoplasma are pathogenic remains to be determined. The pathogenic *Mycoplasma bovine genitalium* has been reported from semen from bulls with seminovesiculitis.^{1b,23,57} Viruses including enteroviruses, genital fibropapilloma virus, foot and mouth disease virus,^{32a,45} *Chlamydia*, epivag, parainfluenza III virus, and IBR-IPV virus have been recovered from the semen or testes of bulls. Freezing semen for the preservation of sperm cells will also preserve most infectious agents including viruses.^{6a,b,47,84,112} Liquid nitrogen used for the storage of frozen semen may also become contaminated with a variety of organisms and viruses and thus be a source of infection for the cow. Bulls clinically infected with Johnes' disease usually have the organism in the semen.⁷⁵

Similar types of organisms as well as those responsible for venereal diseases in each species may also be found in other male animals, for example **Br. suis** in

swine, **Br. canis** in dogs, **Br. ovis** in sheep, *Trypanosoma equiperdum* (dourine) and possibly influenza and infectious equine anemia viruses and the herpesvirus of coital exanthema in horses. A vaginitis and vulvitis are commonly observed in heifers or cows after natural service, especially to older bulls caused by ureaplasma and possibly **H. somnus**. Mares may become infected with streptococci, *Klebsiella* and *Pseudomonas* organisms by being bred to stallions that have large numbers of these organisms in the sheath or semen.

Except for vibriosis, brucellosis, IBR-IPV and trichomoniasis, infections in most cows transmitted to them by natural breeding are not serious and seldom prevent conception or cause subsequent abortion. Many bulls with a seminovesiculitis may have nearly normal conception rates. However, in artificial insemination the author and others have observed several bulls with **Ps. aeruginosa**, **C. pyogenes** or *M. bovine genitalium* infection of the vesicular glands that caused a rapid loss of motility of the spermatozoa probably due to the inflammatory products in the ejaculate. The presence of pus in stallion semen caused a much more rapid decline in motility of the spermatozoa than occurred in normal semen.³⁷ *Pseudomonas* was recovered from semen of 25 of 70 stallions.⁵⁹ No lesions were observed in the stallions, no leukocytes were present in the semen and conception rates were comparable to stallions not harboring the organism. However infected stallions could produce genital disease in mares having a lowered resistance to infection.

In the collection of semen samples for bacteriological or viral studies it is essential that strict sanitary and hygienic practices be observed. Even if the semen is collected in a sterile vagina, contamination usually occurs. Taking a bacteriologically sterile semen sample in the artificial vagina or by electroejaculation is impossible because of contamination from the urethra, prepuce, penis and air. The method of taking a satisfactory sample of secretion from the accessory glands for culture as described in the discussion on seminal vesiculitis is most satisfactory. Briefly this consists of exteriorizing the penis and after careful washing and disinfection of the exposed penis, sheath and lower portion of the urethra, a sterile cannula is passed up the urethra and a sample is collected in a sterile vial by massage of the accessory glands. At present this test is seldom used except to determine the causative agent of inflammatory processes of the upper reproductive tract or accessory glands.

Disease Control in Bulls and Semen—Many studies over the past 40 years on micro-organisms that may contaminate semen and, like spermatozoa, survive processing, freezing and storage and result in transmission of disease have been reported in this and prior Chapters on infertility in female animals and have been recently re-

viewed in respect to cattle.^{6b,c,108b,c} The world wide use of bovine artificial insemination requires herd owners, veterinarians and regulatory officials be cognizant of the current status of these infectious organisms for cattle.

The semen-borne pathogens may be classified into four control-related categories of:

1. **Specific pathogen-free category** requiring the elimination of these organisms from the AI stud followed by routine testing: viruses of foot and mouth disease and rinderpest and *Mycoplasma mycoides* (contagious pleuropneumonia), *Mycobacterium bovis*, *Mycobacterium paratuberculosis*, *Brucella abortus*, *Leptospira* spp., *Campylobacter fetus venerealis* and *Trichomonas fetus* (The last three organisms are treatable. Further studies on improved diagnostic tests for *M. paratuberculosis* are indicated.)
2. **Control by surveillance category** requiring frequent serologic tests of bulls, cultures of semen and close clinical observation to recognize these organisms in a bull or stud: viruses of BVD-MD, IBR/IPV/IPB (infectious bovine rhinotracheitis, infectious pustular vulvovaginitis, infectious pustular balanoposthitis), parainfluenza, fibropapillomatosis, blue tongue, bovine leukemia, Chlamydia, Bedsonia, and *Coxiella burnetii*. [Although as stated previously in this Chapter and in a recent review,^{117b} there is no evidence that the bovine leukemia virus (BLV) present in lymphocytes of serologic-positive, infected animals can be transmitted venereally by natural or artificial service or embryo transfer. Because of the potential for such transmittal many countries importing semen or cattle from the United States require that such donor animals and imported cattle be free of the infection based on the agar-gel immunodiffusion test.]
3. **Control by Sanitation/hygiene** of ubiquitous, opportunistic pathogenic or nonpathogenic organisms including: *Pseudomonas aeruginosa*, *Corynebacterium pyogenes*, *Staphylococcus* spp., *Streptococcus* spp., *Escherichia coli*, *Proteus*, *Mycoplasma bovis*, *Mycoplasma genitalium* and *bovis*, ureaplasma, molds, yeasts and others.
4. Further control of organisms in the above 3 categories may be enhanced or made more certain by the addition of antibiotics to semen for the following organisms: *Leptospira*, *Campylobacter*, *M. bovis*, *Mycoplasma genitalium* and *bovis* and other susceptible organisms in category 3. (This is accomplished by adding penicillin, dehydrostreptomycin, polymyxin B, sulphate and possibly lincomycin, spectinomycin and minomycin in various combinations and concentrations to the extended semen.)

To realize the strict control or elimination of these infectious organisms from bovine semen a number of rig-

idly enforced procedures of quarantine, isolation, routine serologic testing of bulls and culturing of semen and even certain vaccination practices may be required.^{6b,c,108b,c} If artificial insemination becomes wide spread in other species as it has in cattle, similar in depth studies of the infectious organisms and diseases transmitted in semen would be necessary.

Total solids in the bull semen may be rapidly determined and those samples with less than 4 to 5 percent solids, often indicative of incomplete ejaculation or seminal vesiculitis, should be closely examined.^{20,42} Normal ejaculates from fertile dairy bulls averaged 8.8 to 10.0 g. of solids per 100 g. of plasma. Semen obtained by electroejaculation averaged 2.0 to 6.7 percent solids and semen in older bulls averaged 8.9 percent solids compared to 10.2 percent solids in young bulls.

Enzyme determination of semen plasma has proven of limited value in measuring degrees of damage to sperm cells before ejaculation and during the freezing process. Enzymes such as GOT, LDH, cholinesterase and alkaline or acid phosphatase and others are intimately related to the sperm cell. When the sperm cell dies these enzymes pass into the plasma. The levels of enzymes are highest in the bull, intermediate in the stallion and lowest in the boar.⁴⁹

Other tests for semen quality and fertility—in particular rapid tests that would be of value in determining the fertility of semen used in artificial insemination—have been developed and tried. These laboratory tests include those that measure the resistance of spermatozoa to temperature shock, hypertonic salt solutions, or to other inimical influences, and tests for measuring the fructolysis or oxidation rate of semen. The methylene-blue reduction test based on the dehydrogenase activity of semen was found to be closely correlated with motility and concentration.⁹ Other biochemical tests for semen quality were developed and reported by many workers and reviewed.² But as stated by Mann, "On the whole, the metabolic processes in semen are more often related to sperm density and motility than they are to the fertilizing power of spermatozoa." Semen evaluation is indicative for, but not a test of, fertility in a male animal.

Conclusions on the Assessment of Semen Quality as it is Related to Fertility. Excellent reviews and summaries of much published data have been presented^{7,15,25,27} on the relationship of semen quality to fertility in the relatively fertile males present in artificial insemination bull studs. Many semen quality tests and evaluations have been reported by many workers on known sterile or infertile males from which certain general conclusions can be drawn. Extensive surveys of semen quality in populations of males of known and unknown fertility have been performed in bulls,^{29,74} in stallions,^{12-14,35,83} in

rams,^{39,50,60,61} and in men.^{44,80-82} But fewer controlled studies have been conducted such as those in rams where semen examinations of males were followed by fertility trials in an evaluation of the factors of semen quality that were related to fertility or infertility in males.^{61,109}

Differences have long been observed between males in their apparent fertility. Bovine and porcine artificial insemination of numerous females have emphasized these differences. In a recent report 18 bulls from 7 AI organizations were used artificially in a 2500 cow dairy. Five low-fertility bulls, 7 medium-fertility bulls and 6 high-fertility bulls had conception rates of 38, 56 and 66 percent, respectively. The minimum number of 36 services was needed to determine correctly the level of a bull's fertility.³⁴

Another method for assessing the fertility of male animals, that has been shown not to be highly correlated to various semen examinations but is more accurate, is the **competitive matings** between two males in which equal numbers of spermatozoa from each male are mixed and inseminated into the same females (heterospermic matings). Thus differences in fertility of males can be determined using fewer females.^{8,38,102} This method is particularly useful in boars because the large number of offspring requires fewer females in the trial.⁸⁵

The **non-return rate of bulls** used in AI studs is a valid method for assessing fertility between the bulls and a basis for eliminating the bulls with low fertility. However a more rapid and reliable method of fertility prediction is desirable. In one report²⁸ 160 beef heifers were synchronized and superovulated and bred artificially to 8 sires, 5 of which were consistently above and 3 consistently below the average 68 percent nonreturn rates. The heifers were slaughtered 3 to 4 days after insemination and the ova were recovered and examined. The fertilization rates of the ova from the heifers bred to the above and below average fertile bulls was 89 (355 ova) and 70 percent, (155 ova), respectively.

In another similar study⁸⁹ with superovulated heifers bred to 7 bulls with specific morphological sperm cell defects compared to heifers bred to 4 normal bulls the percent of fertilized ova were 33 vs. 72, respectively.

From the above references several generalizations can be made concerning the relationship of semen quality tests and fertility in relatively fertile males used in bovine artificial insemination. The physical activity of semen was more closely related to fertility than was metabolic activity but both were closely related to each other. Presently it is doubtful if more than 20 percent of the differences in fertility can be accounted for by these semen quality tests especially in artificial insemination bulls where the fertility of bulls usually is in a narrow range

of 15 percent difference in conception rates from the most fertile to the least fertile bull. In most cases very poor quality semen resulting in a nonreturn rate of less than 45 percent would be evident and be discarded by the laboratory tests routinely used for semen evaluation.⁷⁷ For this reason in artificial insemination centers good fertility results are based on providing each cow a certain number, about 6 to 10 million, of actively motile spermatozoa. Dead, or immotile spermatozoa have no effect on the normal viable spermatozoa. For an ejaculate to be satisfactory for use in bovine artificial insemination it must have a volume of at least 2 ml. and be of normal consistency and color, a sperm cell concentration of over 500 million per ml., motility of at least 40 percent with distinct progressive movement of cells, less than 15 percent primary abnormalities and a pH of 7.0 or below.

The close correlation in swine between conception rate and litter size is well documented¹¹⁶ and further confirms observations made with uniparous species that there is a wide and definite range in fertility between males. Young, 8 to 12 month old boars should produce 80 to 150 ml. of gel-free semen, opalescent to milky in color, 60 percent motility, less than 10 percent primary defective sperm cells, less than 10% secondary sperm abnormalities and more than 10×10^9 (10 billion) spermatozoa per ejaculate. Older boars will produce to to 400 ml. of semen and have about 10 percent more abnormal sperm cells.⁶⁶ Breeding on 2 consecutive days of estrus will increase conception rates 10 to 25 percent and an additional 4 to 8 percent if different boars are used.⁶⁴

Only a certain minimum quality for each semen trait is needed for maximum fertility. Once this threshold has been reached the association between fertility and semen quality is nearly random, but below this threshold the correlation between fertility and semen quality is important. The semen quality tests most correlated with fertility in males are the concentration or numbers of spermatozoa, the percent of motile spermatozoa and particularly the rate, degree or vigor of motility.

In rams the combined physical examination including the palpation and serologic test for epididymitis due to **Br. ovis**, the assessment of libido and semen evaluation has been closely correlated to the fertility of the ram. When the fertility of rams was categorized on the basis of semen scores as very good, good, satisfactory, poor and very poor and rams in each category were bred to adequate numbers of fertile ewes, the percentage of rams in each category achieving an 80 to 100 percent conception rate was 94, 97, 97, 35 and 25, respectively.^{60,61,88} In 31 rams the scrotal circumference, which ranged from 31 to 42 cm., and semen tests were not related to fertility. However the rams with the highest

conception rate on first service sired significantly more lambs 1.04 vs. 0.89.⁸⁸ Thus, as in swine, the higher the fertility of the male the larger the "litter" size. Rams with satisfactory to very good fertility had 60 to 90 percent motile sperm cells with a moderate to high degree of vigor and progressive movement, 70 to 90 percent live normal spermatozoa and sperm cell concentrations of 1.0 to 1.8 billion/ml.⁶⁰⁻⁶² Rams with poor fertility on the basis of actual fertility trials had 15 percent or less motility with no progressive movement and little or no activity of the spermatozoa, 40 percent or less normal live spermatozoa with sperm cell concentrations of 0.1 billion per ml. or less. No male should be permitted to score higher than his poorest semen character.

About 6 percent of range bulls had poor fertility and 7 percent had questionable fertility based on essentially the same above BSE criteria for semen quality but also including a careful physical examination.²⁹ One report on 29 bulls with normal or satisfactory semen averaged 60 percent conception, range 14 to 100 percent, to the first service, bulls with questionable semen quality had a 48 percent conception rate, range 31 to 57 percent, on first service; and 11 bulls with poor or unsatisfactory semen had a 30 percent conception rate, range 0 to 69 percent, on first service.⁴⁰

In another report, forty 2-year-old Santa Gertrudis bulls were evaluated for breeding soundness. Each of the bulls was exposed to 100 cyclic Santa Gertrudis heifers for a 4 day breeding period with about 12 to 27 estrous females available to each bull. The percent of pregnant estrous females and percent of mated females was recorded. Libido was positively correlated with the percentage of pregnant females in estrus but the scrotal circumference, the spermatozoan abnormalities or motility was not significantly correlated with the conception rates of estrous or mated heifers.¹⁰⁹ In a third report beef heifers bred to 12 Angus bulls with apparently similar semen quality by single or multiple services each estrous period had a conception rate of 62.1 and 62.9 percent, respectively with a range of 0 to 95 percent in single sire matings.⁷⁸ In multiple (3) sire matings the conception rate in the heifers was 74 percent, with a range of 68 to 84 percent, or significantly higher than single sire matings. Except for the one bull, the breeding soundness evaluation tests had low correlations with the conception rates and fertility in the other 11 bulls which ranged from 12 to 95 percent. If the least fertile bull and most fertile bull were removed, the remaining 9 bulls had conception rates ranging from 61 to 80 percent.⁷⁸

If the first semen test reveals poor semen quality, subsequent tests seldom show any improvement except possibly in very young immature males or males recently

affected with a severe stress or disease. However in valuable males with poor quality semen a number of tests including breeding trials over a period of 6 months to one year may be indicated before the male is pronounced infertile or sterile. If semen collected by means of electroejaculation is of poor quality at least 3 more samples at weekly or greater intervals should be collected and evaluated especially if no physical defect is detected. Even then the ejaculator and the collection technique should be checked carefully. Evaluation of semen of range bulls, rams and possibly range stallions, is desirable before the breeding season because these males may collect and guard a "harem" of females and if they are sterile or infertile the pregnancy rate is greatly reduced even if an adequate ratio of males to females is present.

Several recent reviews on the fertility evaluation of stallions recognized that no single test is adequate, that infertility can occur in the presence of normal numbers, motility and morphology of spermatozoa in the ejaculate and that conversely stallions having poor semen quality are able to produce satisfactory conception rates if properly managed.^{71,100,122} As a practical guide to what would constitute a normal fertile stallion it was concluded that the stallion would have to demonstrate normal libido, mating behavior and ejaculation. His reproductive organs should be visibly and palpably normal and free of inflammation or signs of infection or disease. He should be able to ejaculate 400×10^6 (4×10^9) sperm cells in a first ejaculate during the breeding season with 50 percent motility and 60 percent normal morphology.¹⁴ The motility should not drop below 10 percent in fresh semen after 6 hours at 22° C. If a stallion meets these criteria he may be considered a satisfactory potential breeder. If he is borderline in 2 or more criteria or definitely unsatisfactory in 2 or more criteria or has serious permanent disabilities or imperfections he should be considered either a questionable or unsatisfactory potential breeder.^{71,100} However in a stallion the ultimate definition and prediction of fertility, as in other males, is the conception rate after breeding to normal healthy mares in a properly managed breeding program. Sterility or complete failure to settle any of a number of fertile mares is rare in stallions, probably about 3 to 5 in over 5000 Thoroughbred stallions.¹⁰³ Probably very few stallions physically acceptable as breeders would have a failure of libido or complete sterility due to chromosomal abnormalities.

Only males with azoospermia or necropermia should be pronounced sterile. Even if the semen quality is poor, if normal motile spermatozoa are present in sufficient numbers conception can occur. This is especially true in boars, stallions and dogs where the ejaculate is delivered

into the uterus at coitus and the few motile cells more readily gain access to the uterine tubes. In the other species, cattle, sheep, and humans, larger numbers of motile spermatozoa appear to be required as many are lost in the vagina and never traverse the cervix to the uterine cavity.

There is probably no single criterion aside from actual breeding tests that can be used as an accurate overall measure of sperm quality. All facets of the examination of a male should be considered in the evaluation of his fertility including the physical examination, his sex drive and ability to mount and copulate readily, and the examination of his semen. Other considerations might well include the male's genetic merit and his freedom from disease.

As a result of the widespread use and benefits of artificial insemination in the dairy and beef and swine industries, progeny testing of young males is providing needed genetic information to guide farmers and veterinarians in their selection of sires. The "genetic profile" of bulls maintained by progressive AI organizations includes information on production of milk or meat, type and conformation, especially of the feet, legs and udder, disposition, ease of calving and anomalies or defects of their offspring. Additional information is available on the fertility (conception or nonreturn rate) of the males. The above "genetic profile" could be significantly improved by the addition of several other items, with a genetic component, namely: liveability of a male's offspring including stillbirths and postnatal deaths (within one month) and the incidence of twinning and cystic ovaries in a bull's daughters which are of the causes of concern in certain dairy herds.

Such above significant genetic information obtained by extensive progeny testing, which is necessary for the improvement of a breed or species, is regrettably not generally available for the selection of sires in the other species of domestic animals.

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Chapter XIX

ARTIFICIAL INSEMINATION

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Artificial insemination, using the semen of highly selected males, has been the most powerful tool for livestock improvement ever available to the breeder. In the early days of development many books were written on the subject. However, other than in dairy cattle,¹³ there have been no recent treatises on the subject. Consequently, some historical perspective will be included here. Added information can be found in older texts and several recent reviews.¹⁻¹⁵

History

Isolated cases of artificial insemination of domestic animals have been reported for centuries. In the fourteenth century an Arab was alleged to have taken semen by means of a pledget of cotton from the vagina of a mare recently bred to a famous stallion; then by inserting this cotton into the vagina of his own mare conception was produced. Leeuwenhoek and Hamm observed spermatozoa as early as 1677.¹² The first scientific research in artificial insemination of animals was performed on dogs in 1780 by the Italian scientist, Spallanzani. This was confirmed in 1782 by Rossi. Although Spallanzani demonstrated that the fertilizing power of semen resided in the spermatozoa, few further studies or attempts at artificial insemination were conducted until the latter part of the nineteenth century. Heape reported that a dog breeder, Millais, between 1884 and 1896, artificially inseminated 19 bitches, of which 15 produced young. Isolated cases of artificial insemination in the horse about this time also were reported. In the early 1900's workers were beginning to realize the possible value of artificial insemination. In 1907 Ivanov reported the successful results of a series of artificial inseminations in mares, cows, and ewes as a means for the widespread improvement

of farm animals. As a result a laboratory was established in Russia and several hundred men were trained in the techniques of artificial insemination prior to 1914. Japanese researchers also were particularly active during this period. After the first World War, activities in this field in Russia increased greatly and by 1938 the number of animals inseminated in that country was reported as 120,000 mares, 1,200,000 cattle, and 15 million sheep. In 1936 Sorenson and Gylling-Holm organized the first cooperative artificial breeding association in Denmark and by 1958 nearly 100 percent of the cows in Denmark were bred artificially.

Artificial insemination was first performed on cattle in the United States in 1937 and 1938 at the Agricultural Experiment Station in Minnesota. The first cooperative cattle artificial breeding association was organized by E. J. Perry in New Jersey in 1938, with Dr. J. A. Henderson as the first veterinary technician.

Artificial insemination in dairy cattle grew rapidly. In 1956, 21 percent of the dairy cows in the U.S. were bred artificially; in 1969 about 52 percent or 8,000,000 cattle, including 750,000 beef cattle, were bred artificially. Most smaller AI organizations in the U.S. merged into a few large ones. By 1982 artificial insemination had plateaued for several years at about two-thirds of the nearly 11,000,000 dairy cows. Only about 4% of the beef cows are inseminated artificially. Several countries, including Denmark, Japan and Israel breed nearly 100 percent of their dairy cattle artificially. In species such as cattle, where frozen semen is readily available, semen is currently being shipped by air throughout the world.

Artificial insemination in swine has been developed and used extensively in Europe, the middle east and Asia.⁷ Only about 20,000 sows are inseminated in the U.S. Artificial insemination in horses has received widespread attention, but has limited commercial use. The development of frozen semen in horses and the newer therapeutic methods for the control of estrus and ovulation could increase the use of artificial insemination in the future.

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Advantages and Disadvantages

The advantages of artificial insemination are well known, and greatly outweigh the disadvantages; if this were not so, the rapid growth of the artificial insemination would not have continued.

1. Artificial insemination greatly increases the utilization of proven sires. The services of outstanding, superior sires are made available to many more owners. Milk production has doubled since artificial insemination was introduced through better genetics, feeding and management.^{3,15} This has been of economic benefit to the owner and the country. Many proven bulls have artificially sired between 100,000 and 200,000 calves in their lifetime. This use of outstanding sires is further increased by the ability to ship frozen semen of some species worldwide. Stallions potentially may sire over 100 foals in a short breeding season. Boars may sire over 1,000 litters of pigs per year.

2. Bulls used in artificial insemination are more carefully and scientifically selected from outstanding cows and proven sires than is possible in individual dairy herds. Computers scan the records of all the top tested cows and matings are made with the best sires available. About 90 percent of the possible genetic improvement in a commercial herd depends on the genetic improvement through artificial insemination. Artificial insemination permits earlier and more rapid proving of young bulls on a greater number of cows under varied conditions. This gives a more accurate proof of a male's transmitting ability than can the testing of a bull on only one small group of females in a herd under similar conditions of management and feeding. This mode of testing also distributes the risk so that inferior bulls cause little loss to individual owners. In bull studs it costs about \$10,000 to prove the genetic worth of a young bull even when his initial purchase price may be small. Because only about one out of seven to ten bulls tested is usually kept as a proven sire, each of these represents an average investment of about \$75,000.

3. The danger, work, and expense of keeping and handling, what in many cases proved to be, an inferior male is eliminated for the average dairyman. This added saving by the use of artificial insemination can be spent on maintaining an additional cow, which, may defray part or all of the yearly cost of breeding a herd artificially.

4. If the males are handled carefully, examined closely from a health standpoint to make certain that they are free from disease, if regular semen examinations are made and accurate breeding records maintained, artificial insemination lessens or eliminates the occurrence of ve-

neral diseases such as vibriosis, trichomoniasis, and brucellosis. Large A.I. organizations are members of the National Association of Animal Breeders and they routinely test their bulls for a battery of diseases (see Chapter XVIII). When semen is obtained from a member of the National Association of Animal Breeders, one can be assured that bulls have been carefully screened for disease. Because only high quality semen is shipped to breeders, conception rates can be improved if the semen is handled properly and the cows are bred at the proper time. Artificial insemination frequently results in improved record keeping, and in heightened interest on the part of the farmer in having cows conceive promptly. This has been helpful in the early diagnosis and treatment of genital abnormalities and has often resulted in an improved breeding efficiency in the herd. In herds affected with vibriosis and trichomoniasis, artificial insemination, may be a valuable means or aid in overcoming the disease. In fact, in herds using artificial insemination for many years, vibriosis and trichomoniasis are not found. In an emergency, such as an outbreak of foot and mouth disease, previously stored frozen semen can be used safely by an A.I. Stud.

5. With the advent of the widespread use of frozen semen and the classification of the physical characteristics of a proven sire's daughters, careful selection of bulls for type and line breeding is possible for the breeder who so desires.

6. The intensive selection and record keeping has reduced the incidence of lethals and other genetic defects.

7. Miscellaneous advantages of artificial insemination include the following:

a) It makes possible the mating of animals with a great difference in size without injury to either animal.

b) It may extend the usefulness of sires which for some physical reason are unable to copulate normally.

c) It may be used to increase the usefulness of males of monogamous species such as the fox. It is of value in experiments on hybridization where natural mating cannot take place.

d) Artificial insemination usually stimulates greater interest in livestock breeding and in better management practices.

e) Artificial insemination has proved to be of value for male dogs that are timid or have premature erection, as complete erection of the canine penis does not ordinarily occur until after entry into the female's vagina. In toy breeds of dogs it may be used to prevent exhaustion due to repeated attempts to copulate during hot weather. It may also be of value in relatively impotent male dogs.

f) It may be helpful when used in females which are in true estrus and ovulate but refuse to stand or ac-

cept the male. An example of this is in zoo animals where pairs refuse to mate. Semen can be collected by electroejaculation, frozen and used when the female is in estrus.

The disadvantages of artificial insemination should be recognized and carefully considered.

1. Well-trained operators are required to supervise the collection, examination, extension, freezing, shipping, and the insemination of the females in order to ensure that infectious diseases such as brucellosis, vibriosis, trichomoniasis and others are not spread. All major A.I. organizations in the U.S. maintain studs free of these diseases. If semen is not collected, extended and handled properly, poor breeding efficiency results. Careful observations for estrum and insemination at the proper time is important. Careful, complete records must be kept. Inseminators, if they are not careful, could be a means of spreading infectious diseases from one farm to another.

2. There is a possibility of spreading genetic abnormalities in cattle, such as: cystic ovaries, spastic syndrome, poor conformation, especially of feet and limbs, and lack of libido. However, large artificial insemination organizations have systems for routinely evaluating udder, legs, feet and other type traits. Only those sires passing this evaluation are used to produce sons for further testing. The increase in cystic ovaries in dairy cattle may be due partly to the wide use of certain bulls by means of artificial insemination. Improved feeding practices and successful treatment of cows with cystic ovaries also may have increased the incidence of cystic ovaries.

3. Miscellaneous disadvantages:

a) Intrauterine insemination of a pregnant female may result in abortion.

b) Uncontrolled or unscrupulous operators or owners could substitute sperm of less valuable animals unless blood typing is routinely employed. However, few errors have been found, so this seems to be a minor problem.

c) Service is not always available. Many dairymen take training to do their own insemination.

d) Artificial insemination cannot be used conveniently on all species or breeds of animals. In some species much more work must be done before artificial insemination becomes practical.

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AI in Cattle: General and Liquid Semen

Few advances in livestock production have been so rapidly accepted and have had such a profound influence on dairy cattle improvement as has the use of artificial insemination. The ability of bull semen to be stored for long periods and the confined management conditions under which dairy cattle are kept, have made artificial insemination very adaptable to this segment of the livestock industry in the United States and other countries. Artificial insemination has been commonly used on valuable purebred beef cattle, especially on small farms or in foundation herds. It provides a convenient means of crossbreeding. Because of the large number of beef cattle scattered over a large area when on range, the principal problem and cost is that of finding cows during estrum and driving them to a central point for insemination. Most ranchers prefer to let the bull manage re-

production, despite its many disadvantages. Methods of synchronization of estrus may increase numbers of beef cattle inseminated. At present many owners of larger farms are breeding artificially to their own bulls using frozen semen or they are purchasing semen from other sources.

The collection of semen from the bull for use in artificial insemination is usually accomplished with the artificial vagina and occasionally where necessary with electroejaculation as described in Chapter XVIII. Semen collected by personnel experienced with electroejaculation equipment is comparable in quality to that collected by the artificial vagina. The concentration of spermatozoa per ml by electroejaculation often is about one-half that of semen collected by the artificial vagina, but the volume of semen is twice as large. The pH usually is higher. Thus, the motility of the spermatozoa and the total numbers of sperm cells per ejaculate were the same for the two methods of collection, and this is most important. Semen collection from Brahman and Santa Gracudas is difficult as they are shy. With proper management most mature bulls in artificial insemination studs may be collected up to four times weekly over an extended period of time.

It is important to have a properly designed place for semen collection, providing safety for the handlers as well as for the bull. Good footing is important. Proper restraint of teasers and a place to sexually prepare a bull with more than one teaser can facilitate obtaining the best semen possible. Only bulls, steers or dummies should be used for mounts and these should be cleaned or covered between each semen collection to prevent any possible transmission of disease among bulls. All collection equipment should be sterilized and aseptic techniques of semen collection used. Obviously, only bulls with excellent reproductive characteristics producing high quality semen should be selected for A.I.^{10 and 1-15}.

Semen Evaluation

This is covered in Chapter XVIII. However, it should be mentioned here that all major suppliers of semen collect and examine semen carefully.¹⁹ Each ejaculate must pass a test for semen volume, sperm motility, sperm concentration and general appearance. Frozen semen must meet rigid motility standards after freezing and thawing. Various more detailed tests are included with problem bulls. Semen that is contaminated should be discarded. Most semen collected from mature bulls trained to serve the artificial vagina should have at least 50% of the spermatozoa motile and a concentration that usually exceeds 500 million/ml.

Liquid Semen

Handling the semen after collection is very important. It should not be allowed to cool below 20° C without adding medium such as buffered egg yolk or heated milk to avoid coldshock.^{11,13,15} The dilution of semen with proper extenders protects against coldshock and prolongs the viability and fertility of the spermatozoa. Cooling the semen from body temperature of about 38° C to 5° C over a period of two hours should be done in protected containers placed in a coldroom at about 5° C.¹³ The extender should include penicillin, streptomycin and polymyxin B.^{2,6,7,11a,20}

Extenders for Liquid Semen. Most bull semen for commercial use is frozen. However the extenders used for frozen semen were modified from liquid semen extenders, primarily by adding the cryoprotectant, glycerol. Consequently, brief coverage of these extenders will provide a background for the discussion of frozen semen.^{1,3,5,9,14,15,18,21,25,26}

A semen extender should have the following characteristics:

1. Provide nutrients.
2. Protect against the harmful effects of cooling (coldshock).
3. Be buffered at the proper pH for bull semen of about 6.7-7.0.
4. Have the proper osmotic pressure and balance of ingredients.
5. Inhibit bacterial growth.
6. Increase the volume (dilute the sperm cells) without reducing sperm cell viability.
7. Protect sperm cells during freezing. A common cryoprotectant is glycerol.

The most common extenders contain either **egg yolk** or **milk**. Buffered egg yolk extender was first described by Phillips and Lardy in 1940 who used a phosphate buffer with egg yolk. In 1941 Salisbury et al. described the egg yolk citrate buffer extender which presently is widely used with glycerol as an extender for frozen semen. This extender made possible the rapid advance of artificial insemination. The egg yolk citrate diluter is prepared by adding 2.9 gms of sodium citrate dihydrate ($\text{Na}_3\text{C}_6\text{H}_5\text{O}_7 \cdot 2\text{H}_2\text{O}$) to 100 ml of double distilled water and mixing it at a rate of one part egg yolk to one to five parts of buffer solution. To prepare the egg yolk for the buffered egg yolk extender, fresh eggs should be washed in water and wiped with 70 percent grain alcohol. After allowing the egg to dry, the shell is broken with a sterile knife in a dustfree room. Egg yolks are separated from the egg white aseptically. The protective value of the egg yolk is largely due to the lecithin and

lipoproteins.^{8,13} Most extenders are prepared fresh each day in artificial insemination centers.

Egg yolk-tris also has been used widely for liquid and frozen semen.^{11c} The buffer is made with 24.2 grams of Tris, 15 grams of citric acid monohydrate and 12.5 grams of glucose per liter of double distilled water. To this 20% egg yolk (1 part egg yolk:4 parts of Tris buffer) is added, along with penicillin, streptomycin and polymyxin B. This extender has been used for frozen semen by adding about 7% glycerol by volume. With this extender, semen extension and filling of straws can be done at room temperature before cooling, thus being more comfortable for the laboratory personnel.

Boiled, pasteurized, homogenized milk, and boiled, pasteurized skim milk^{1,3,18} have been reported to be as satisfactory as the buffered egg yolk extenders as an extender for bull semen. These extenders are prepared by placing fresh homogenized or skim milk in the top portion of a covered Pyrex glass double boiler and heating it to 95° C or 203° F. The thermometer is removed, the lid replaced to avoid water loss and gentle boiling is continued for ten minutes. The boiling period should not be excessively prolonged. The boiled milk is cooled to the same temperature as the semen to be diluted. The milk can be filtered or poured slowly from the boiler leaving the surface scum of albumin on the sides of the boiler. No unboiled or improperly heated milk should be added to the boiled milk, as relatively small amounts of unboiled milk exert a harmful effect on spermatozoa. Copper-lined utensils should not be used. Ordinary fresh pasteurized milk or fortified skim milk has not proven as satisfactory as pasteurized homogenized or skim milk as a semen extender and their use is not recommended. The milk can be boiled the day before use and stored in a refrigerator. The satisfactory use of 9 percent homogenized sterilized cream was reported.¹ Skim milk powder, if of a good grade, may be used in preparing a satisfactory extender.¹⁸ The toxic fraction in milk is apparently the lactenin that is destroyed by heating.³ The protective fraction is composed of the phospholipids. It is easier to view sperm in skim milk but whole homogenized milk often is used.

Controlled fertility trials reported by various workers using egg yolk buffer and milk extenders have been summarized.^{8,13} The results with both extenders on the same ejaculates of semen were similar.

Antibiotics added to semen extenders have been shown to increase the viability of spermatozoa and to eliminate *V. fetus* organisms in the extended semen.¹⁷ It was found that 1,000 units of penicillin and 1,000 micrograms of streptomycin per ml of extender had no adverse effect on the spermatozoa and effectively con-

trolled bacterial growth in the diluted semen.² The addition of antibiotics to semen of low-fertile bulls improved their conception rates 10 to 15 percent.^{11a} Foote et al.^{11a} compared the combination of penicillin, streptomycin and polymyxin with individual antibiotics and obtained the best results with the combination. This is still the presently recommended combination of the National Association of Animal Breeders. This definite improvement in conception rates was possibly due to better control of vibriosis found to be present in the semen in many older bulls^{17,20} (see Chapter XIV). Five hundred units of penicillin and 500 micrograms of streptomycin per ml were found to be as satisfactory as the higher concentrations if semen was extended at least 1:25 times and held for 6 hours before use.¹⁷ Non-contaminated buffer solutions containing antibiotics for the egg yolk extender may be stored for one week at 5° C. For liquid semen extenders sulfanilamide may be added at a concentration of 0.03 gms per ml. Sulfanilamide should **not** be used for extenders for frozen semen. Excessive levels of antibiotics in semen may be toxic to spermatozoa and amounts above those recommended have no additional beneficial effect.

It should be noted and emphasized that although antibiotics will eliminate some bacteria in semen such as *V. fetus*¹⁷ and reduce the numbers of certain susceptible bacteria such as streptococci and staphylococci it will not eliminate such organisms as *C. pyogenes*, *Brucella* spp., *Trichomonas fetus*, *Leptospira* spp., mycoplasma, *Mycobacterium tuberculosis*, *Pseudomonas*, *Listeria*, and viruses such as IBR-IPV, *Chlamydia*, epivag, and others. Freezing of semen to which antibiotics have been added will further preserve nearly all of the above organisms for long periods of time.

Other antibiotics have been tried in semen extenders,^{8,13,6,7,27} and some are definitely harmful while others were no better than the penicillin and streptomycin combination. Currently many others are under test, particularly those which may control mycoplasma.²⁴ The addition of antibiotics to semen cannot be a substitute for the careful, sanitary collection of semen with a low bacterial content from healthy disease-free males.

Modifications of the above egg yolk buffer and milk extenders that have shown possible advantages include the addition of:

Catalase, at a level of 20 to 100 mg per ml,¹⁴ affords protection to extended semen, especially in yolk citrate buffers. Catalase prevents the formation of hydrogen peroxide due to the effect of light⁹ and agitation on semen, but its effect on fertility was not significant.¹⁵

Enzymes (with the possible exception of amylase), hormones, tranquilizers, vitamins, glucose, fructose, and other substances have been added to extenders without

noticeable success in improving the fertility rate. Amylase added to semen has been reported to increase conception rate, but its possible beneficial effects were not repeatable in other trials.^{11b}

VanDemark and co-workers^{25,26} described a modified egg yolk buffer semen extender in which carbon dioxide was bubbled through the buffer solution until the pH reached 6.3. The diluted semen was sealed in ampules and stored in the dark at room temperature. Although the results were inconsistent, some workers reported good conception rates for up to 7 days.

Foote et al.¹⁵ described an improved semen extender called C.U.E. (Cornell University Extender) that contained one part egg yolk to four parts of a special buffer containing sodium bicarbonate, potassium chloride, glucose, glycine, sodium citrate and antibiotics. This gave 66% pregnancy rates. However this extender is not good for freezing semen.

Extending Semen

The extension rate of semen is designed to give the optimal sperm per insemination dose. In practice this usually is the minimum number consistent with maintaining maximum fertility. By determining the volume of an ejaculate of semen and sperm cell concentration per ml., one can calculate the number of ampules or straws that can be filled with a standard number of sperm cells per breeding unit. The percentage of motile spermatozoa also is considered. Good quality bull semen, as ejaculated, should have at least 50% motile sperm and a concentration of 500 million sperm per ml.

Work by Foote and others^{11,13,14} indicated that 5 million motile sperm per ml. was about the minimum insemination dose when one ml was used for insemination. The 60 to 90 day nonreturn rate was 75 percent, with a pregnancy rate about 10 percent lower. If a sample of semen was 7.0 ml, had 60% motile sperm and a sperm concentration of 1,500 million sperm per ml., this would be enough to inseminate 630 cows with 10 million sperm per cow. With 5 million sperm per cow the total possible number would be 1260. Extension rates with liquid semen as high as 1 part of semen to 200 parts of extender were common. In New Zealand the cows are inseminated with about 2.5 million freshly collected sperm in the short breeding season.

Excessive light should be avoided during semen processing. This can cause photooxidation which is harmful to the sperm cells whether they are to be used with or without freezing.⁹

When numbers of spermatozoa per insemination decreased from 10 to 6 million there was a 0.5 percent drop in conception rate per each million decrease.²⁸ When one

breeding unit (one ml) of extended semen contained fewer than 6 million spermatozoa there was a decrease of about 2.6 percent for each million decrease in spermatozoa. When not all of the semen is needed for use, the dilution rate to control vibriosis should be at least 1:25 and the semen should be in contact with the antibiotics for at least 6 hours.¹⁷

After the gradual cooling period, the semen is extended by adding a calculated amount of extender, also at refrigerator temperature, 35 to 45° F or 3 to 8° C, to bring the amount of previously slightly diluted semen to the final volume needed. The semen and extender are gently mixed by tilting the container back and forth.

Nearly all bull semen today is processed for freezing. However, when liquid semen was used the extended semen often had colored coal-tar dyes added to aid in identification of breeds.⁴ Each bull was carefully identified on labeled tubes and the semen was packaged and kept at 3 to 8° C until used or discarded. Best fertility was obtained within 48 hours of collection.

A veterinarian could prepare his own egg yolk-citrate, egg yolk-tris or more conveniently boiled milk. This can be frozen in aliquots and stored.¹⁶ Selected references to the earlier literature on liquid semen are included to indicate the variety of combinations of balanced ingredients that were used successfully.^{8,12,13}

Thus, on an average farm, a semen sample would be collected, 1 ml of semen would be added to 25 ml of diluter, or 1/2 ml semen to 12 1/2 to 15 ml of diluter. Even if the sperm cell concentration were only 500,000 per ml, this would still provide over 10 million spermatozoa per ml if only 60 percent were actively motile. Proper antibiotic concentrations may be added to this small amount of prepared extender by making a stock solution of 100,000 units of crystalline penicillin and 100,000 micrograms (100 mg) of dihydrostreptomycin in 10 ml of a citrate buffer solution. To obtain a final concentration of 500 units or micrograms of each antibiotic per ml of egg yolk buffer or milk extender, 0.5, 1.25 or 2.5 ml of the antibiotic stock solution should be added to 10, 25, or 50 ml of extender, respectively. To obtain a final concentration of 1,000 units of each antibiotic in the extender the amounts of the added stock solution should be doubled. Although it is possible for a dairyman to manage his or her own A.I. program, they must be very skillful in estrus detection and all aspects of reproductive management.⁸

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Frozen Semen

For many years frozen semen has largely supplanted liquid semen for artificial insemination of cattle in the U.S. and around the world.¹

The chief advantages of frozen semen are:

1. More efficient year round use can be made of semen from proven or injured sires.
2. Selected matings can be made at any place at any time to a large number of available proven sires. Custom freezing of semen makes frozen semen available from farmer-owned bulls. The latter also can be a disadvantage when bulls are not carefully screened genetically or for disease.^{4,5,6,65}
3. Semen can be stored for months to many years at -320° F (-196° C) in liquid nitrogen as a refrigerant. Frozen semen has been reported to have a slight decline in fertility^{38,70} after long-time storage. This was probably due to problems of handling in the field, as semen kept continuously at -196° C does not decrease in fertility for years.^{18,25}
4. Shipping costs are reduced from the bull stud to the technician in the field because semen supplies and liquid nitrogen supplies only need replenishment about once a month. Semen may readily be shipped anywhere in the world.²³
5. Great care is taken by major suppliers of frozen semen to insure that each package of frozen semen is carefully labeled and controlled.²⁰

6. Sperm cell output, percentage of morphologically normal spermatozoa and percentage of motile sperm after freezing was lower in bulls 6 to 12 years of age than in bulls 3 to 6 years of age.³⁰ Thus semen quality was highest in bulls not yet old enough to complete the progeny test. It might be desirable in certain young bulls with lower quality semen to freeze a supply before it reached an older age and the semen becomes relatively infertile. Banking of semen¹⁸ is followed on some bulls, particularly those breeds with few cow numbers.

The major disadvantages of frozen semen are:

1. Semen from about 10 to 20 percent of the bulls does not freeze well. These are often bulls with poor semen quality and low fertility even if semen was used in liquid form.

2. In the freezing process about 40 to 50 percent of the spermatozoa are killed so increased numbers of spermatozoa per insemination are required.^{23,28,64} When a proven sire is in great demand fewer cows can be bred compared to extended liquid semen. However, 6 to 8 million motile sperm after freezing are sufficient per insemination.^{16,17,54,55}

3. If proper bull health is not maintained, frozen semen has great potential for the spread of viral and bacterial diseases. Major bull studs are under continuous health tests.³³

4. Heavy use of frozen semen could limit the number of sires used, and possibly result in narrowing the genetic base of a breed. However, the actual increase in exchange of semen possible with frozen semen also has increased the number of sires used to produce sons, so this has not happened generally.

History

In 1949 Polge et al.⁶² reported that spermatozoa of several species, including cattle, could be treated with glycerol and survive at a temperature of -79°C . They showed that the protective action of glycerol, by modifying the type of crystal formed during freezing, resulted in less harm or injury to the cells and thus survival of spermatozoa could be greatly improved by the slow cooling and freezing process which they perfected. In 1951 the first calf was reported born from insemination with frozen semen. Thereafter interest in the application of frozen semen spread rapidly. Additional calves were born in England the following year. The first calf in the United States resulting from the use of frozen semen was born in May, 1953. The early work with frozen semen used solid carbon dioxide ("dry ice") as a refrigerant at -79°C . Extensive studies by American Breeders Ser-

vice resulted in the development of liquid nitrogen storage units which were very efficient and prolonged the storage life of spermatozoa.⁶¹ Details of the development of frozen semen and other associated historical events have been published.³⁴ Today it is clear that genetic material may be preserved in the form of properly frozen sperm cells for a lifetime, probably for centuries and perhaps for milleniums.

Extenders for Freezing Bull Semen

Bull semen for freezing is usually processed in an egg yolk-citrate, or an egg yolk-tris or milk extender.^{8,19,23,28,73} The milk can either be skim milk or homogenized whole milk. These extenders are prepared the same way initially as for liquid semen (see previous section). However, before freezing glycerol is added in various ways (described later) so that this cryoprotectant is present during freezing. Also, in a few countries where semen is processed in pellets, a sugar solution (lactose or raffinose) is combined with 20% egg yolk by volume plus 4 to 5% glycerol for freezing semen.^{49,50}

Extending and Cooling Semen

When semen is collected it is about 38 to 40°C in the collection tube. It is protected against the cold and usually brought into the semen processing laboratory at about 37 to 38°C . The semen is placed in a water bath at 35 to 37°C . Raw semen has antibiotics added in concentrated form at this point to provide maximum effect against microorganisms which may be present. The recommended concentrations of antibiotic are added in a volume of .02 ml to each ml of raw semen—so as to give 1,000 IU of penicillin, 1,000 ug of streptomycin and 500 ug of polymyxin B per ml.

Then the raw semen is mixed about 1 part of semen with 3 to 4 parts of any of the extenders listed previously. Whatever extender an A.I. organization has had most experience with they should continue to use under normal circumstances. However, one study indicates that much less than 20 percent egg yolk may be necessary.⁷³ It is important that the semen and extender be the same temperature when they are combined. The two parts should be mixed thoroughly by gentle swirling or inversion of closed tubes. This mixture often is referred to as the Pre-X (pre-extended semen). It is placed in a water jacket at the same temperature to protect against rapid cooling. The unit is placed in the coldroom at about 5°C where cooling takes place over a period of about 2 hours. After this time it is brought to one-half of the final volume with the same extender as used previously, excepting the antibiotics sometimes are reduced to about 500 units of penicillin, 500 ug of polymyxin B and 500

ug of streptomycin per ml. Up to this point no glycerol normally has been included, except in extenders containing tris buffer.

One-half the final volume without glycerol provides an opportunity to add glycerol slowly using a similar extender containing double the final concentration of glycerol by adding a volume equal to the first half. The actual volume of extender required depends upon the number of sperm cells available in the collection. This collection may represent more than one ejaculate from a bull. For example, two ejaculates collected the same morning may be combined after cooling and processed as one collection.

Supposing there are 10 billion motile cells in the collection from a particular bull and it is estimated that 50% of these cells will survive freezing and thawing. Thus, we would expect this collection to have 5 billion motile sperm after freezing. If the goal was to have 10 million motile sperm cells per breeding unit (straw, ampule or pellet) this would make potentially 500 breeding units. Of course, a small percentage is lost in processing, so the actual number of breeding units would be slightly less.

Assume that semen is being processed for the 0.5 ml straw. This is very common in the U.S.A., although there also are straws holding about 0.25 and 0.3 ml of semen.^{35,48,57} When packaging in 0.5 ml straws the 500 straws represent 250 ml of extended semen. So the first half of the extended semen without glycerol would be 125 ml. Then 125 ml of extender, usually containing about 14% glycerol by volume, would be added dropwise or stepwise over a period of about 30 minutes.

Another way of calculating the straws that could be filled with 0.5 ml and the volume of extender required would be as follows: Supposing the 10 billion motile cells, to start with, was made up of two ejaculates combined as one collection totaling 10 ml. This collection had 70% motile sperm with a sperm concentration of 1.428 billion cells per ml. This would be 1.000 billion motile sperm per ml. If freezing will kill 50%, there will be 500 million motile cells after freezing. Each straw with 0.5 ml has 10 million motile sperm per straw packaged at a concentration of 20 million motile sperm per ml. The arithmetic is quite simple, as 500 million divided by 20 million is a 25-fold dilution. Then 10 ml of semen diluted $25 \times$ gives 250 ml, one-half of which is without glycerol and the final one-half added with glycerol.

The actual number of sperm per ml varies with organizations and demands for semen from particular bulls. Usually it is desirable to extend semen at a rate to give 6 to 12 million motile sperm per breeding unit.^{16,23,54,55,60} High extension rates also reduce numbers of contami-

nating microorganisms, reducing the chances for infection.

Equilibration time is the period needed before freezing for the sperm cells to become adjusted to the extender so that upon freezing excessive loss of sperm cells does not occur. This time varies greatly between species. It is not necessary that bovine sperm cells equilibrate with or be in the presence of the glycerol for a period of time before freezing. Recent experiments, including fertility trials have indicated that the semen should be in the extender with or without the glycerol for about 4 hours at refrigerator temperature. Because of the adverse effects of glycerol on antibiotics, equilibrating for at least 4 hours in glycerol-free extender is desirable.¹⁰ The second half of the egg yolk extender should contain about 14 percent glycerol by volume, making a final dilution rate of 7 percent. If sterilized milk is used as the extender the second half of the extender should contain 14 to 20 percent glycerol so the final concentration will be 7 to 10 percent. Glycerol should be added gently by dripping or in small increments, usually in the cold room. The diluted semen is then placed in 1 ml amounts of glass ampules or more commonly in 0.5 ml straws that are sealed after being filled. Freezing should be accomplished within 4 to 20 hours of collection of the semen. A recent study¹⁰ reported on bull spermatozoa from 10 bulls exposed at 5° C to extenders containing glycerol for 6 hours, 30 minutes and 10 seconds before freezing. The latter very short equilibration time resulted in a highly significant improvement in sperm motility following freezing and thawing. More study is obviously indicated especially since the Milk Marketing Board in England reported that 6 highly fertile bulls whose semen following freezing had poor conception rates could be improved by a shorter equilibration time.

Freezing Semen

Freezing rates vary depending upon the kind of extender used. The principle is to freeze as rapidly as possible to avoid the osmotic shock of water freezing out (thereby increasing the salt concentration), but **not** so fast as to cause marked thermal shock with intracellular ice formation.^{28,64}

Freezing is usually done in liquid nitrogen freezers. The temperature is lowered from +5° C to about -100° C in 8 to 10 minutes by controlling the flow of nitrogen vapor over the straws or ampules. Ampules freeze a little more slowly than do straws. Anytime after the semen reaches -100° C it can be placed directly into the liquid nitrogen for storage at -196° C.

This storage temperature was preferable to dry ice at -79° C⁶¹ so liquid nitrogen is used almost universally.

Semen can be stored for years at -196°C .²⁵ Normally there is no point in storing semen longer than necessary to use it for insemination. An exception is to preserve certain banks of germ plasm. However, frozen embryos may be used for this purpose.

It is very important to keep frozen semen immersed in liquid nitrogen. This way there is no chance that semen will be warmed at all during storage. This aspect, along with thawing will be discussed further, under shipping and handling.

Ampules and Straws

The first sealed packages for freezing semen were ampules which held 1.0 ml of extended semen. These have been largely replaced with straws holding from 0.25 to 0.5 ml. The advantage of the straw over the ampule is that the sperm cells can be frozen more uniformly, and less storage space is required. In fact storage is greatly increased with the .25 ml straw. A typical field unit which would hold 1,512 1 ml ampules will hold up to 3,000 0.5 ml straws. Also, fewer sperm are left in the straw than in the ampule upon insemination.

All major suppliers of semen run quality control checks on semen after freezing. If it has been stored for a long time they check it again for the percentage of progressively motile cells. Normally semen must have 25% or more progressively motile sperm cells to be shippable.

Some sperm cells are killed in freezing and the general viability of sperm when incubated after freezing is not as good as before freezing. Nevertheless the conception rates with frozen semen are only slightly below those achieved previously with liquid semen. A 60 to 90 day nonreturn rate of 74.5 percent was reported¹⁷ with control liquid semen. Frozen semen stored 1 day and 103 days at -79°C resulted in nonreturn rates of 72.7 and 71.0 percent, respectively. Semen frozen, thawed and subsequently shipped for use 24 to 60 hours later averaged only 51.7 percent nonreturns. Most bull studs today are averaging just a little under 70 percent 60- to 90-day nonreturn rates with sperm frozen in straws and stored continuously in liquid nitrogen at 196°C . A comparison of ampules and straws with about 8 million motile sperm per insemination dose showed the nonreturn rates for straws was slightly higher than for ampules, but the difference was not significant.⁵⁴ A review of the fertility of semen packaged in straws and ampules⁵⁷ slightly favored the straw.

Freezing in Pellets

The extender for the pellets is composed of lactose, 11 percent, or raffinose, 18.5 percent in distilled water and 20 percent egg yolk, 4 to 5 percent glycerol, and

antibiotics.^{49,50} About 3 parts of warm extender are added to semen at 35°C and cooled to 5°C in about 1.5 hours. Three or four hours are provided for equilibration. About 0.1 to 0.2 ml of the extended semen containing 12 to 30 million spermatozoa is put directly in depressions made in a block of dry ice for 5 minutes to freeze. Then the pellets are transferred to storage tubes and put directly into liquid nitrogen. The pellet usually is thawed just before use in 1 ml of 3.2 percent sterile sodium citrate solution at 35°C . Then it is handled for insemination as liquid semen.

The advantages of such techniques are: the obvious savings in cost of storage and sometimes better survival of sperm from bulls whose semen freezes poorly otherwise. At present these methods lack automation and are slightly cumbersome. Sanitation is questionable and contamination in the liquid nitrogen is theoretically possible with pellets of semen. Identification methods for the semen are not as good as with ampules and straws. However, techniques have been developed for freezing the code number of the bull printed on thin paper as a part of the pellet.

Antibiotics added to semen to be used in the liquid or frozen form has limited value against most pathogenic organisms often present in the semen. As mentioned previously, penicillin at levels of 500 to 1,000 units and streptomycin at levels of 500 to 1,000 micrograms per ml. of liquid semen extended 1:25 or more times and stored for 6 hours before use controlled *V. fetus* present in the sheath and semen of bulls. Semen from infected bulls when treated with penicillin and streptomycin, extended, frozen in the usual manner and stored for one week before use was unable to produce infection in susceptible cows.^{39,44} Later it was shown the addition of polymyxin B sulfate (see previous section on use with liquid semen) at a level of 500 units per ml of extended semen along with 50 units of penicillin and 2,000 micrograms of streptomycin controlled *V. fetus* in the semen.²¹ The extended semen was incubated at 37°C for 30 minutes before cooling and freezing. The protozoan, *Trichomonas fetus* can remain viable and infective especially in liquid extended semen, but also in frozen semen containing antibiotics. The chances of survival of the organism are markedly reduced in semen containing glycerol and experiencing a long equilibration period before freezing. *Br. abortus*, *Listeria monocytogenes*, *C. pyogenes*, *L. pomona* and other such organisms are not affected by the antibiotics at levels that can be used in either liquid or frozen semen.^{40,42,47} Of course the viral agents of disease that may be in semen such as IBR-IPV and others are not affected by antibiotics added to the semen. Therefore, it is imperative that bull studs main-

tain bulls free of brucellosis, tuberculosis, trichomoniasis, leptospirosis, vibriosis (campylobacteriosis), and virus diseases. All major artificial insemination organizations carry out extensive disease control programs. New antibiotic combinations² are being tested to assist in controlling the presence of possible organisms such as mycoplasma.⁷⁷ For the individual owner of purebred bulls, used both naturally and artificially, and employing custom-freezing and for persons using such semen, the problems of disease control are complex. They are difficult to overcome even with highly competent veterinary and laboratory service.

Freeze-drying of bovine spermatozoa, as is employed extensively for the storage of bacteria at room temperature has been attempted by a number of workers but without reproducible success.⁴⁶

Shipping and Handling Semen

This discussion is limited to frozen semen as so little semen is shipped in any other form. The only exception is the use of highly extended liquid semen during the short breeding season in New Zealand. Also, if a specimen is obtained for diagnostic purposes it could be extended, cooled to 5° C, packed with a bottle of ice at 3 to 5° C and brought to a Diagnostic Laboratory. Frozen semen can be transported by car, truck, bus, railroad or airplane. Most A.I. organizations have trucks carrying frozen semen and liquid nitrogen. They resupply distributor or inseminator tanks, or on-the-farm units about every 4 weeks. Some of the newly engineered tanks will hold liquid nitrogen for several months, depending upon the model and conditions of use.

Semen handling in the field is very important.^{12,58,69} The tank should always contain several inches of liquid nitrogen. Preferably it should be filled whenever the nitrogen tank is half empty. The semen should be organized with a well arranged inventory.⁷¹ This avoids having to pull canes of semen out far enough to check the bull number and possibly damage the semen. **Never pull a canister or cane of semen above the edge of the liquid nitrogen tank** to remove a breeding unit of semen. Never take more than 15 seconds to remove the unit wanted. If possible, keep the goblets containing straws filled with liquid nitrogen so that they will be surrounded by the nitrogen even in the neck of the tank. Always return the canister back to the lower level position in the tank as soon as possible. Never thaw out more ampules or straws than will be used within 15 minutes of thawing. Most problems with poor semen quality result from improper field handling of semen. Large A.I. organi-

zations have extensive quality control procedures and a reputation they protect by insuring that all semen leaving their premises is of high quality.

Thawing of semen for insemination is very important.^{58,68,69} The optimal rate depends upon the kind of extender used for freezing. One should follow the recommendations of the semen supplier in thawing the semen. Some who use milk extender recommend a pocket thaw. Thawing time is the time required to thaw frozen semen in a water bath at about 30° C. Most organizations recommend a thaw bath of 35 to 40° C. Automatic thawing devices that plug into cigarette lighters in cars have been developed. Straws will thaw in less than one minute. Ampules take several minutes to thaw.

Once the semen is thawed it should not be loaded into a very cold gun in a cold barn. The inseminating gun can be warmed slightly with the hand under cold conditions before covering with a sterile sheath. Then insemination should proceed promptly. This avoids any possible freezing of the semen after thawing which would be damaging to the sperm cells. A slight amount of cooling does not seem to be detrimental. Nevertheless it is always good practice to avoid warming, cooling and re-warming frozen-thawed semen.

If there is any doubt about how well the semen has been stored, it should be checked microscopically for the proportion of motile sperm cells. If fertility is poor this check is most important. Some semen from individual bulls may have passed through the storage tanks of several distributors. It is especially important to check the quality of this semen, particularly if it has been purchased at a premium price.

In countries or areas where liquid nitrogen is available, several manufacturers¹ provide excellent insulated tanks at a cost of \$300 to \$700 which hold up to several thousand breeding units. Smaller tanks are used for shipping frozen semen. Old tanks require refilling with liquid nitrogen every 4 weeks, depending on their size and frequency of use, and some newly designed tanks may be safe for 4 months between refills. Thus, semen may be shipped long distances by air or other means of transportation over a period of several days.

Semen is a living biological product and could carry such diseases as foot and mouth disease and other cattle diseases.^{3-6,40,42,65} Health regulations have been established in certain states and in most countries regarding the importation of semen.^{3,4,33} For those desiring to import or export semen, information and permission should

1. Cryogenic Engineering Co., 4595 Bannock St., Denver, CO 80216; Linde Co., Div of Union Carbide Co., 270 Park Ave., N.Y.C. 10017; Minnesota Valley Engineering, Inc., New Prague, MI 56071.

be requested from either the Animal Inspection and Quarantine Division, Agricultural Research Service, U.S. Department of Agriculture, Washington 25, D.C. or from the Federal or State Veterinarian located in each state. Each semen shipment must be accompanied by the proper official health charts to comply with the regulations of the country of its destination. Semen shipped intrastate usually has no restrictions placed on it unless the herd is under quarantine for an infectious disease.

Successful insemination of the cow depends upon (1) the quality of the semen used, (2) proper storage and handling of the semen, (3) a cow being reproductively healthy and in estrus and (4) use of proper insemination procedures.²⁷ Following is a discussion of the latter two points, as the first two were discussed previously.

The **optimal time to inseminate** a cow is from the middle to the end of estrus.⁷⁶ This is about 6 to 24 hours before ovulation, as discussed in Chapter XIV. With good detection of estrus near optimal conception rates were found by Foote²⁶ following the so-called A.M.-P.M. rule. Cows first seen in estrus in the morning were best inseminated the afternoon of the same day. Cows first seen in estrus in the evening should be inseminated the next morning. Conception rates were lower when cows first seen in estrus in the evening were not inseminated until the next afternoon or cows first seen in estrus in the morning were not inseminated until the next morning. In another study²⁹ cows were inseminated when first seen in heat versus a delay of 12 hours when the next heat check was made. This did not result in a statistically significant difference in conception rate. However, the pregnancy rate at the early insemination was 48 percent versus 53 percent for the insemination 12 hours later. Cows still in estrus 12 hours after insemination had a 57 percent conception rate as compared to 48 percent for those not in estrus 12 hours later. Pregnancy rates for heifers and cows in first, second, third or fourth and more lactations were 59, 51, 49, 48 and 38 percent, respectively. Ambient temperatures below 10° C or above 23° C at the time of insemination were associated with a decline in pregnancy rates. As sperm live in the cows reproductive system for 30 hours^{8,13} there does not seem to be a specific optimum time to inseminate. Also, in practice the exact time of onset of heat usually is not known. Nevertheless, with frozen sperm which do not survive as long in a test tube after freezing and thawing, it is thought that a slightly late insemination may have better chances of initiating pregnancy than an earlier one. Semen placement also affected fertility.^{41,78}

There is no doubt but what the whole aspect of cow management at insemination is important. Increased pregnancy rate occurred in beef cattle by applying cli-

toral massage immediately after insemination.⁶³ This has been confirmed with other studies in beef cattle. The technique did not affect fertility in dairy cows.⁴³

Many diarmen inseminate their own cows. If professional insemination service is not available this may be desirable. The diarmen feels that the insemination can be better timed.⁷⁹ However, it is then important for the owner to perform large numbers of inseminations and keep in practice, because many studies reveal that this is essential for best semen placement. Also, it is important that the semen inventory and liquid nitrogen level in the semen tank be carefully maintained.^{71,72} Under these circumstances the tradeoffs of convenience or inconvenience of doing one's own inseminations and conception rates that may be achieved probably balance out. But if herd fertility is low and a person on the farm is doing the inseminations, one of the possible problems is insemination techniques or improper storage of semen. This is much less likely to be the case with a professional full-time inseminator, especially if good results are being achieved in surrounding herds serviced by the same person.

Regardless of who does the insemination, the procedure is very important. One should be well-organized and have all equipment ready when thawing the semen. Thaw the semen according to the directions of the supplier. This usually will be at a temperature around 35° C. Then proceed carefully. NAAB has a checklist for new inseminators.

A comfortable clean place to restrain the animal for insemination also is important. An atmosphere of calmness is important. Sanitation also is important.³⁷ By carrying out hygienic procedures the inseminator protects the semen, the cow and himself or herself. One should not allow any contaminating materials to come in contact with the inseminating gun. The cow should be approached gently.

At the present time nearly all cows are being inseminated by the operator inserting one hand and arm encased in a rubber or plastic glove and sleeve into the rectum and grasping the cervix. Excess fecal material is paddled out. The vulva and vulvar lips are carefully wiped or, if necessary, washed and then wiped dry with cotton or a paper towel, precautions being taken to make certain that no feces are wiped between the vulvar lips. An inseminating pipette, such as the Cassou gun for straws, is inserted through the vulva dorsally and forward through the vagina and into the external os of the cervix. If folds of the vaginal wall interfere, the cervix is pulled or pushed forward to straighten the lumen of the vagina. If the external os is hard to locate, the cervix may be held by the fingers and the thumb placed over the external os; the

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 pipette is manipulated to touch the thumb and then into the cervix. By a combination of gently inserting the pipette and working the cervix over the pipette, it is usually readily passed one-half to two-thirds of the distance through the cervix, or into the uterine body on first services. The semen should be deposited slowly over a period of about 5 seconds. The body of the uterus is very short, so the objective is to deposit the semen on first service just through the cervix.

There has been general acceptance of the placement of the forefinger over the cranial end of the cervix on first service. As soon as the tip of the inseminating gun touches the finger, stop. Most technicians tend to inseminate too deeply. A variety of studies with dye placement and x-rays have been carried out. In one study only 42 percent of the inseminations were in the anterior cervix or body of the uterus, 42 percent were in the right horn and 4.4, 7, and 3 percent were in the left horn, posterior cervix and anterior vagina, respectively.^{57a}

Although there was no significant difference in the conception rates between the cervical or uterine body deposition of semen, semen deposition should be in the cervix when cows appear to be in diestrus, pregnant, or the cervix is otherwise difficult to pass. Intrauterine insemination could result in endometritis and a shortened cycle (Chapter XIV). If insemination occurred during the luteal phase of the cycle it could cause pyometra. Furthermore if non-motile organisms such as *Br. abortus* are placed in the cervix they do not readily become established in the uterus.⁴² The endometrium of the uterus may be injured by the pipette causing an abscess of the uterine wall. The intrauterine deposition of semen could result in abortion in pregnant cows.^{66,74,75} As many as 10 percent of pregnant cows, especially the first three months of pregnancy, show estrus.⁷⁴ Lastly, intracervical deposition of semen is more easily and quickly accomplished than is intrauterine deposition.

If semen is deposited into the uterus on first service it should be placed in the body or in both horns, or the ovaries should be examined to detect the location of the mature follicle and semen placed in the corresponding horn. This latter procedure requires great care not to rupture the follicle manually as this is usually followed by a failure to conceive. Most inseminators require about 2 to 3 months to become adept at inseminating cows. Each person should inseminate at least 500 cows to achieve high competence under different conditions. There is a significant difference between technicians and their insemination results. Conception rates may vary from 15 to 20 percent between technicians depending on their attitudes, methods of handling the cow, timeliness of insemination, care of handling semen, their techniques of

insemination and the method of record keeping.⁵⁸

Traumatization of the cervix is unnecessary and dangerous. If the pipette will not pass readily into the cervix due to its small size in virgin heifers or due to pathologic lesions or defects, the operator should make certain that the animal is in estrus, and, especially if it is a heifer, the semen should be deposited as far into the cervix as the tube can be gently or readily passed. In such instances it is probably desirable to use larger amounts of semen as some may be lost into the vagina. Using a pipette of smaller diameter might be helpful. The straw inseminating gun is smaller in diameter than the older plastic rods. Complete obstruction of the cervix or uterine horn is characterized by mucometra. It has been reported that penetration of the cervix with a pipette was not possible in 1.1 percent of 11,112 cows and 11.7 percent of 1,711 heifers, but conception on A.I. service occurred in 36.5 percent and 54 percent of these animals, respectively.⁵²

For good conception rates in herds bred artificially close cooperation and consultation is necessary between a competent veterinarian, a good herdsman, owner or manager, and the A.I. technician. If the herdsman, owner and A.I. technician are the same person then one has fewer people observing the animal. The herd should be placed on a routine reproductive examination program accompanied by good records that are reviewed periodically. Regular prebreeding or postpartum examinations of cows, pregnancy examinations, twice daily careful heat checks and records, prompt treatment of reproductive abnormalities of the estrous cycle and genital tract, and insemination of cows at the proper time of estrus with highly fertile semen are all important parts of a complete reproductive health program. With increasing herd size this becomes even more important. A good manager will find that no other program will pay greater dividends.

Measurement of the success of the insemination, such as regular pregnancy diagnoses, are important for the dairyman, inseminator and veterinarian in herd health and A.I. programs. It is also important for the semen supplier to be able to evaluate fertility of bulls and compare A.I. technicians they employ. Pregnancy results (palpation per rectum) are usually not available for this purpose. A nonreturn rate has been developed in A.I. to provide a regular basis for evaluating the reproductive efficiency of bulls and technicians.⁷ This nonreturn rate measures the proportion of cows inseminated which have not been resubmitted (returned) for another insemination within a certain time. For cows inseminated in a particular month, the nonreturn rate after two to three months (two months from the end of a particular month and three months from the beginning) is known as a 60- to 90-day

nonreturn rate. A faster cutoff in time at 30- to 60-days after insemination or with a fixed cutoff interval can be programmed easily with the high speed computers used today. Typical 60–90 day nonreturn rates with liquid semen for first services were in the low 70's and with frozen semen run just below 70.¹³ Second service cows have about the same nonreturn rate and pregnancy rate as first service cows, but conception rates decline with successive services in repeat breeders. There has been some concern that repeat inseminations with a foreign protein, such as egg yolk could cause immune reactions and infertility. However, studies⁵⁵ indicate that this is not a problem.

The submission of breeding records to an A.I. organization is essential for calculating nonreturn rates and this can provide relatively accurate information.⁵³ Nonreturn rates are higher than true pregnancy rates resulting from a particular insemination.^{7,45,53} This is because some cows are sold that are not pregnant, cows are rebred to a bull or some other source of semen is used. Because more and more semen is sold directly to herds and distributors, where there is no feedback, the fertility of semen used and general success rate achieved by an organization in the field is less well established. A.I. organizations do a rigorous quality control on semen, and this becomes more important as less reporting of fertility occurs. A.I. organizations that continue to employ their own full time inseminators have an advantage in this regard. They can maintain accurate records to compare bulls and inseminators.

Special fertility testing may also be done. Various experimental procedures are being researched to evaluate the fertility of bulls in highly efficient designs requiring fewer cows. One of the techniques is to use competitive fertilization.⁵¹ In this test semen from 2 to 3 sires is mixed and the proportion of progeny from each sire is determined later. Either color markings or blood type must be used to identify which sire produced the sperm that resulted in the calf. These types of tests require special followup and are not used with registered cattle. Some *in vitro* tests, using zona-free hamster eggs, to estimate the fertilizing ability of bull sperm or sperm from other valuable males of domesticated species are promising.

Artificial insemination in range beef cattle, if it is to be successful, requires excellent management and following practices to which many ranchers are unaccustomed. The principles are the same as for dairy cattle. Cattle in the herd are usually bred artificially with frozen semen for a period of 24 days, slightly longer than one normal estrous cycle, or preferably 45 days, two estrous cycles, with semen from a proven beef bull. The technician must be experienced. The cows or heifers to be

bred must be placed in a fairly level lush pasture confined area, free of bushes and trees and gullies so cows in estrus can be easily observed. Cows must be well fed during the last part of the previous pregnancy as well as after calving. Heifers nursing calves may require added grain or forage so that estrus will occur regularly. At least 3 pens large enough to hold 5 percent of the herd in each pen should be built near the water supply or where cattle are accustomed to feed. Connected to these pens should be a chute to hold 6 to 8 cows with a step-in gate to allow the technician access to the cows. Well-trained and experienced ranch hands who will handle cattle quietly should examine the herd carefully early in the morning when the cows first move about and again in the late afternoon or early evening. Otherwise many heats will be missed. One rider can usually observe about 200 cows in a good pasture arrangement. During the middle of the day beef cows are usually rather inactive.

Beef cows in estrus are much more quiet than dairy cows and ranch hands should observe that cows in heat tend to group together, may be nervous and walk around, tails may be slightly elevated, and mucus may be present at the vulva which may be edematous. They tend to stand behind other cows. Mounting in beef cows is much less frequent than in dairy cattle so it is harder to note cows standing to be ridden. Often the periods of estrus in the southern states and in Brahman or Zebu cattle are shorter than the estrous periods in the English beef breeds in the more northern states. Cows in estrum should be hazed slowly into the corral and holding pens for breeding. Cows must be identified and records maintained of the dates of service and the bull used. Long hard hours plus careful attention to details are highly important to good conception rates in beef cattle.^{13,14}

The use of "teaser" or vasectomized bulls has not generally been very satisfactory although some ranchers have reported success with them. The presence of a bull can increase sexual activity among cows and increase heat detection.⁹ Some use young 3- to 5-month-old beef bull calves; others use vasectomized bulls; while others use bulls with the penis truncated or deviated by various procedures which prevents copulation but does not interfere with libido. Also, a "Pen-O-Bloc," device has been used by some with variable results for detecting estrum. This device in the sheath (which is designed to block protrusion of the penis) is later removed to use the bull as a "cleanup" bull. These bulls are most effective if not allowed to run continually with the herd, but are turned out in the morning or evening whenever heat checking is done. Some ranchers use commercial "heat detector" patches ("Kamar") that may be glued to the sacrum. If the cow is mounted by another cow a dye is released

that can be easily observed. With such detectors on the rump of a cow it is desirable to run heat checking bulls or testosterone-treated steers with the cows continuously to detect cows in estrum at times cows are not observed directly. After two inseminations about 80 to 85 percent of the cows should be pregnant and one "clean up" bull for every 100 head should be turned in to breed the remaining unbred cows.

Estrous cycle regulation, with the objective of inducing animals to ovulate at a preset time has been investigated extensively.^{24,31,32} Many products have been approved for use in recent years. These include the natural prostaglandin $F_{2\alpha}$ (Lutalyse, The Upjohn Company) and analogs of prostaglandin such as "Estrumate." Various progestational agents are available. These include a silastic coil impregnated with natural progesterone (progesterone releasing intravaginal device, PRID), and a synthetic progestogen, "Norgestomet," which is combined with estradiol valerate in a commercially available product called "Synchro-mate B" (Ceva Labs.). There are many other combinations which have been tested.^{24,31} These hormonal treatments are not cures for infertility. However, the progestational agents tend to increase the proportion of suckled beef cows which will be induced to ovulate in the normal postpartum breeding period of about 50 to 100 days. Removing the calf from the mother for 48 hours has been studied extensively by Wiltbank,⁸⁰ and this increases the synchrony and number of cows that can be impregnated in a short period of time. It is very important that animals be well-fed and managed for synchronization to be effective. Recommendations of the manufacturer of each product must be followed carefully. When this is done recent studies indicate that conception rates can be as high as breeding cows and heifers at naturally occurring heats. This is in contrast to the first 20 years of work with estrous cycle regulation, when conception rates in treated groups of animals often were 10 to 20% below controls. As a consequence of current technology it is possible to group beef cattle into a tighter calving pattern and use semen from genetically superior sires by careful application of drugs to synchronize ovulation. These same techniques work especially well with dairy heifers.

Artificial insemination organizations. The large number of 100 or so small A.I. organizations in the U.S. which developed as A.I. first grew in the 1940's and 1950's have decreased due to many mergers.³⁴ Most of the semen today (outside of custom freezing) in the U.S. and Canada is supplied by about 10 large organizations. The proportion of registered cattle resulting from A.I. has increased over the years so that this technology predominates in producing dairy cattle that are registered.

The A.I. organizations and various colleges have intensive training programs to train full-time inseminators as well as herdsman's schools to train farm personnel to inseminate cows. The latter have been increasing, so a substantial part of the semen produced by these few large A.I. organizations is sold for direct service. In the high concentration areas of dairy cattle of the northeastern, midwestern and western parts of the U.S. there are still many full-time inseminators. The development and current status of organizations affiliated with the National Association of Animal Breeders (NAAB) has been described recently.³⁴

A full-time inseminator may inseminate between 2,500 and 4,500 cows per year, depending upon the density of the cow population in the area and the inseminator's reputation as a top performer. Charges for insemination service vary from about \$8 to \$10 per cow, and a second or third service may be free. However, the semen must always be purchased. This cost usually ranges from about \$5 to \$30. Semen from a few bulls highly sought because of pedigree and type, as well as production may be priced considerably higher.

At large bull studs complete uniform and regular health tests and procedures are carried out under the supervision of a competent veterinarian. The National Association of Artificial Breeders in the U.S. has adopted a Health Code of Minimum Standards³³ (obtainable from NAAB), that requires bulls to be negative to the following tests: tuberculosis, once or twice annually; brucellosis, blood tests and semen plasma tests twice annually; trichomoniasis, twice annually; and leptospirosis, twice annually. All bulls should be tested before coming from the farm to the stud; and should be placed in isolation for 4 to 8 weeks on arrival and retested. Many bulls are purchased as calves. If the bull is of breeding age six negative sheath tests for trichomoniasis are requested. For vibriosis control all studs must add the proper amounts of penicillin, dihydrostreptomycin and polymyxin B to the extended semen. Vibriosis should be eliminated from the stud since practical methods have been devised.³⁹ All A.I. studs in the U.S., Canada and several European countries are free of vibriosis (Campylobacteriosis). If a bull develops a blood titer for leptospirosis he should be isolated for 4 months and treated with parenteral dihydrostreptomycin and his blood titer should be stabilized before his semen is used. Many other diseases, particularly viruses are of considerable concern (See Chapter XVIII) to A.I. studs, regulatory officials, cattle farmers, and veterinarians. Many purebred breeders use artificial insemination within the herd to control genital disease and to be able to offer for sale semen from valuable sires. Often this is coupled with embryo transfer to produce

sons for sale and daughters for herd replacements or sale. There is an increasing demand for veterinarians to provide or advise on this type of service.

Further health requirements include general recommendations as to sanitation, investigation into the disease problems of herds of origin of newly purchased males, and elimination of bulls found to harbor genetic recessive defects. As newer knowledge concerning older diseases becomes available and new disease entities that might be spread by semen are reported, steps must be taken by the bull studs to incorporate and use this information to further protect the health of their valuable bulls and the herds of patrons using their semen. This is under continuous investigation. Monoclonal antibodies against viral diseases currently are being studied. In the U.S., custom freezing and uncontrolled sale of semen from bulls in private small herds provides a potential for wide-spread dissemination of infectious diseases. Such bulls are seldom subject to the rigid, continuing health standards enforced in most of the large A.I. studs.

With the growth of the large A.I. organizations and their major investments in genetic testing and disease control programs, the small bull rings have largely disappeared. The large organizations have highly trained personnel, well-equipped laboratories and careful quality control procedures. Thus, these are sources of semen which represent known quality. Another valuable service of the large central breeding units is the detailed recording of the fertility rates of bulls, and the collecting of data on the proof of production and the type transmitted by the bulls, so that intelligent selection of known proven sires can be made. In the large organization this makes possible the development of proven bulls and rapid improvement of the genetic makeup of cows sired by them, providing that participating members recognize the need and value of this service and cooperate with it. For further information on artificial breeding organizations the reader is referred to several of the general references listed earlier.

Blood typing of all bulls used artificially is required by the purebred beef and dairy cattle associations. There are about 70 known antigens in bovine blood of which about 50 are used routinely for blood typing. The combinations of blood antigens possible are so great that no two animals are similar unless they are identical twins. In questionable parentage cases the cow's and her calf's blood are typed. Then by a check of the blood types of the two bulls in question, one of the bulls can usually be excluded. Based on parentage tests 20 percent of cows bred artificially to two different bulls within an eleven day period conceived on the first service, while only 1 percent of cows bred to two different bulls at an 18 to

24 day interval conceived to the first service.⁶⁶ This study suggested that parentage tests are indicated when cows are bred to different bulls on consecutive heat periods, when the intervals between service dates are less than 16 days or when the gestation length from the last service for normal sized calves is shortened 8 to 10 days or more. Blood typing assures the accuracy of pedigrees and the maintenance of the purity of purebreds and has been an important factor in the growth and confidence in artificial insemination of cattle.

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Artificial Insemination in the Horse

Although the horse was one of the first animals successfully inseminated by Ivanov on Russian stud farms early in this century, the practice has not become widespread because of difficulties in storing and shipping liquid or frozen stallion sperm as compared to the sperm of bulls. Also freezing stallion semen reduces fertility considerably, and most importantly there is the problem of detecting and breeding the mare at the proper stage of estrus to obtain a high conception rate. Only a few of the purebred equine breed registries recognize artificial insemination.¹ The Thoroughbred association does not permit or recognize artificial insemination except as it immediately follows a natural service to the same stallion. The Standard Bred Association and American Quarter-Horse Association permit artificial insemination on a farm with fresh unfrozen semen but do not permit transport of semen. Much work over a number of years will be necessary to develop artificial insemination of horses to its full potential. It is not likely to reach the level practised in cattle because of the scattered small horse farms, and the difficulties posed by a long estrous period and in the detection of estrus. Mares do not exhibit homosexual activities during estrus as do cattle. Detection of estrus in mares is best and most easily accomplished by teasing with a stallion.

Artificial insemination has been used to control diseases such as dourine and equine infectious anemia. Other advantages include (1) reduced chance of injuring the mare, (2) correction of bad breeding habits in stallions, (3) the possibility of evaluating each ejaculate of semen, (4) preventing overuse of the stallion (5) aiding in identification of reproductive problems, (6) permitting more mares to be bred to a particular stallion and (7) permitting use of valuable old stallions.¹⁸ If frozen semen can be improved, to have a good supply all the time, mares can be inseminated at the time to yield maximum fertility. Also, mares that have certain physical problems, and whose resistance to infection is low, may be inseminated with semen containing added antibiotics.

Semen collection has been described previously. Stai-

lions can be trained to mount a phantom²⁴ as well as a mare in estrum or one injected with estrogen. Thorough teasing of the stallion and scrubbing of the penis and sheath during the teasing period are important.²⁶ This removes smegma and other debris. Any residual water and soap should be removed with a clean dry towel. The artificial vagina (A.V.)^{11,22} is the best device for semen collection. This equipment, its assembly and use has been described in a preceding chapter and in the general texts cited previously.^{5,8,11,12}

Semen evaluation also was described previously. Care should be taken to protect the sperm from major changes in temperature or exposure to sunlight during examination and while holding until it is used for insemination. The semen may be collected with a strainer or filter, nylon preferred,^{1b} in the A.V. If this is not used the semen should be strained and volume with and without gel recorded. Also, any gross contamination should be noted. In addition the percentage of motile spermatozoa and concentration of sperm per ml should be determined. This information is needed in calculating the volume of semen required to provide sufficient sperm for insemination. In addition, sperm morphology should be noted. However, in contrast to normal bull semen stallion semen often contains more than 20 to 30 percent abnormal cells, even from fertile stallions.

Handling, extending and storing semen should be done gently, avoiding shaking and rapid changes in temperature. Normally, if semen is collected for insemination on the premises it should be collected just before the mares are ready for insemination. Fresh semen then can be used quickly without the necessity of preparing semen extenders and fertility is high.²³ If the semen is to be stored for several hours it should be mixed with an extender and kept in the dark. Sperm in raw semen held at room temperature or higher for 8 hours loses its motility.¹⁵ By mixing semen with extenders at various rates and cooling slowly to 5° C sperm has been used for several days. It was reported that 67 percent of 218 mares inseminated with extended semen conceived while 79 percent of 199 mares handled similarly, but bred naturally, conceived.¹³ The composition of the extender as well as storage time markedly affect conception rates. The number of spermatozoa inseminated also is an important factor. In one study^{9b} the mares were inseminated with (1) "fresh semen" held less than 1 hour at 39° C in a cream-gel extender, (2) semen cooled to 5° C for 2 hours in cream-gel extender, (3) semen cooled as before, but with 7 percent glycerol added and (4) semen held at 5° for 24 hours in cream-gel extender. The pregnancy rates (18 mares per group) at the first cycle were 56, 39, 6 and 28 percent, respectively. After 3 cycles the cor-

responding values were 94, 83, 44 and 56 percent, respectively. While the number of mares per group is too small to pinpoint accurately the conception rate due to each treatment, it is clear that both glycerol and storage for 24 hours were detrimental. Because cream-gel has been reported to be one of the better extenders for preserving unfrozen stallion sperm³³ this decline in conception rate emphasizes the desirability of using unfrozen semen in a relatively short period of time. There are many anecdotal accounts of using unfrozen semen after prolonged storage, but these lack controls and sufficient numbers and information to verify the success rate. This emphasizes the need for substantial research on the preservation of the fertilizing ability of stallion semen so that the most judicious use of desired stallions can be made to obtain maximum pregnancy rates in the mares.

Stallion sperm are sensitive to centrifugation.^{7,9a,25} Under certain circumstances it may be desirable to concentrate the sperm for storage or for freezing. Care should be taken to use low centrifugal forces and it was reported²⁵ that 10% seminal plasma should be retained to preserve maximum motility and fertility.

Also, care should be taken to avoid shaking and agitation of liquid semen that is to be transported or shipped. Tubes should be filled and sealed tightly to avoid agitation and leakage. Plastic bottles of ice in an insulated container should be provided to insure a temperature of approximately 5° C when extended semen is to be shipped long distances.

Equine semen extender—Horse semen, as noted in the previous chapter, is high in electrolytes and low in sugar, and sperm cells survive only a relatively few hours in the seminal plasma. Most recommended extenders that have proven satisfactory have generally supplied sugar and other protective substances. Some recommended extenders for equine liquid semen include:^{13,14,18,27,28,33}

- (1) Sterile skim milk or sterilized mare's milk prepared in a manner similar to bovine sterilized skim milk extender by heating in a double boiler to 92° C for 10 minutes. This extender can be stored frozen.
- (2) Distilled water or sterilized skim milk, to which 7 gms of glucose and 0.8 gms of egg yolk have been added per 100 ml.
- (3) Homogenized sterilized, 9 percent, cream, 400 ml, to which one-half ounce of plain gelatin in 40 ml of water heated to 145° F is added with gentle stirring while both were warm to prevent the lumping of the gelatin. Penicillin (1000 I.U.) and 1000 micrograms of streptomycin per ml are added. This extender can be frozen and stored for several weeks or more.

- (4) Hughes and Loy¹³ used a boiled skim milk diluter for extending semen and inseminating mares up to 24 hours after collection. For storing semen from 24 to 96 hours they used an extender in which "half and half" cream was heated to 95° C in a double boiler for 2 to 4 minutes. The scum was removed and the hot cream was added to 1.3 gm of Knox gelatin which had been autoclaved with 10 ml of distilled water, to a final volume of 100 ml. After cooling these two extenders, 1000 units of crystalline penicillin, 1 mg of dihydrostreptomycin and 200 units of Polymyxin B sulfate were added per ml of diluter. These diluters can be made up in advance and stored frozen in a freezer.
- (5) A dried skimmilk-glucose extender that is quite widely used for storage of stallion sperm for several hours consists of the following: 2.4 gm of "Sanalac" dried skimmilk, 4.9 gm. of glucose, 92 ml. of sterile distilled water, 2 ml. of 7.5% sodium bicarbonate and 2 ml of gentamycin sulfate.
- (6) A cream-gel extender can be simply prepared¹⁸ by adding 1.3 gm. of Knox gelatin to 10 ml. of distilled water, autoclaving and adding to 90 ml. of "half and half" cream which has been heated to 92° C. for 10 minutes in a double boiler. This can be frozen.
- (7) A Tris-egg yolk extender, modified from the bull semen extender, has been used, but fertility was lower than with cream gel.²³ However, all of the Tris-egg yolk extenders contained glycerol, which in several other studies has been found to be detrimental to stallion spermatozoa. Contrary to these earlier reports another study placed centrifuged stallion spermatozoa into a Tris-egg yolk-glycerol extender to remove the seminal plasma.¹⁰ Fertility of semen stored at 5° C was maintained for 2 to 6 days in a limited trial.
- (8) In Germany¹⁷ extensive use has been made of lactose extender modified from the Japanese lactose extender developed originally for pelleting bull semen.¹⁹ The extender has several modifications but consists basically of lactose, egg yolk, sodium citrate, EDTA, sodium bicarbonate, a detergent, glycerol, water and antibiotics (penicillin and streptomycin). It is used primarily for frozen semen packaged as pellets or large volume (4 ml) straws. Best results were obtained when the semen was centrifuged in extender, rediluted and frozen. Twelve of 19 mares conceived on a single insemination.
- (9) There have been many other extenders^{14,20,30} and references can be found listed in those cited. Many

of the reports are based on preliminary laboratory studies without fertility information.

Antibiotic additions to stallion semen have not been studied thoroughly. This is surprising in view of the potential contamination of stallion semen and the use of artificial insemination in mares which appear to be especially susceptible to infection. Equine spermatozoa appear to tolerate antibiotics commonly used for bull spermatozoa,³ such as penicillin, streptomycin and polymyxin B. In addition gentamicin is used widely. Recently amikacin² has been found to be innocuous to stallion spermatozoa. This antibiotic is especially effective against *Pseudomonas* and several other gram negative organisms. It can be combined with selected other antibiotics. It was used successfully to infuse mares before insemination.⁵ Some clinicians report that they infuse mares with extender containing antibiotic a few hours before insemination. This treatment does not seem to have been tested experimentally, but likely has the same effect as other solutions of antibiotics.

Freezing horse semen was first reported in 1957⁴ when epididymal spermatozoa were frozen in sterilized milk containing with 10 percent glycerol. One mare, of seven bred, conceived with frozen semen stored for 30 days. In 1963⁷ a technique of layering equine semen over an extender of sterilized skim milk containing glucose, fructose and egg yolk and centrifuging at 1200 rpm for 7 minutes at 30° C followed by and pouring off the supernatant seminal plasma after 95 percent of the sperm cells had been spun into the extender was reported. Further extender was added and the extended semen was cooled to 4°. Then equal parts of 20 percent glycerol in more extender was added slowly over a period of one hour. The semen was poured into 10 ml. vials, equilibrated for 5 hours and then frozen. Two of 11 mares inseminated with the frozen semen conceived. A similar technique resulted in about 70 percent recovery of sperm motility after freezing but no fertility trials were conducted.²⁸

During the 1960's experimental work with stallion semen was in progress in Pennsylvania, New York, Wisconsin (American Breeders Service) and particularly at Colorado State University, along with studies in Germany. Support for this research has been surprisingly minimal, considering its importance.

The importance of centrifugation is still controversial. If one wishes to store frozen semen in small volumes then concentration is important, and centrifugation is a convenient means of concentrating sperm. Low speed centrifugation is necessary, and possibly the retention of at least 10 percent seminal fluid during freezing is desirable. However, this may depend upon the extender

and method of freezing.^{10,17} By freezing and storing in larger volumes one can avoid concentrating the sperm at all, or it can be partly concentrated by collecting only the sperm rich fraction.⁶ This procedure also has been used by others.²⁹

The amount of cryoprotectant seems to be very important as a detrimental effect occurred in cream-gel within 2 hours of storage.^{9b} In another study¹⁰ 7.5% glycerol did not reduce fertility with unfrozen semen stored in a Tris-fructose egg yolk extender. However, with frozen semen only 1 mare out of 16 conceived during the first cycle versus 70 percent for mares inseminated with unfrozen semen. Only 7 of 16 mares had conceived after 4 cycles when inseminated with the frozen semen. Perhaps glycerol in the freeze-thaw process was more damaging than it was protective. In other studies^{14,17} 5 percent (v/v) of glycerol has been used.

Recently¹⁴ stallion semen extended with a dried skim-milk based extender with 5 percent (w/v) glucose was used to extend stallion semen to 250×10^6 sperm per ml. A portion of the semen was frozen in the lactose-egg-yolk-glucose-ETDA formula.¹⁷ Over one hundred mares were inseminated daily starting at day 2 of estrus, assigned alternately to control or frozen semen. Only 29 percent of the mares inseminated with frozen semen conceived, compared with 66 percent for the controls.

Sperm numbers may have been limiting in the trial just described, as frozen semen contained about half of the number of motile cells compared to the control. Many studies have been done to compare the number of motile sperm inseminated.^{12,21,27,33} In some studies as few as 80×10^6 motile spermatozoa produced as high a pregnancy rate as more spermatozoa. However, with frozen semen 500×10^6 sperm per insemination usually produced a higher pregnancy rate than 50 to 100×10^6 sperm per insemination. Obviously the fertility of the mare and timing of insemination may alter the response obtained with different sperm numbers inseminated. Volume of semen inseminated is believed by some to be important and generally 5 to 10 ml of semen are inseminated. However, when smaller volumes containing adequate sperm numbers are inseminated, fertility is not affected. There is great variation in the fertility of sires^{14,31,32} with frozen semen. Thus, stallions used in fertility testing with frozen semen usually are selected for the freezing quality of their semen. At the present time 300 to 500×10^6 sperm are recommended as an optimal insemination dose. Earlier studies had indicated that a billion or more sperm cells were needed in a volume of 10 to 50 ml.^{1,3,8,9,11,12} With proper detection of estrus and multiple inseminations during estrus, 500×10^6 sperm cells appear to be satisfactory. With skilled management the optimal

number of spermatozoa may be less. For convenience in insemination and to be sure sufficient volume is deposited in the uterus 5 to 20 ml is usually inseminated. With fresh undiluted semen, as is often used on Standardbred and Quarter horse farms, 5 ml of raw semen should have a sufficient number of sperm ($\geq 500 \times 10^6$ sperm) to impregnate the mare.

Insemination of mares. The mare should be in estrus. The characteristics of mares in estrus have been described many times and their quantification relative to the stage of estrus summarized.³² Winking of the vulva, crouching and urination in the presence of a teaser stallion all are positive signs of estrus. Because mares are not homosexual mares will not attempt to mount each other.

Insemination is performed on the second to fourth day. If the mare is still in estrus on the fifth or sixth day, insemination should be performed again. If the stallion semen is of good quality and fertile, insemination need only be performed every 48 hours, because spermatozoa may retain their fertilizing capacity for up to 4 to 6 days in the mare.⁸ By careful teasing, speculum examination of the cervix or rectal palpation of the follicle on the ovary and the cervix, insemination may often be performed when ovulation is expected in 12 to 24 hours. Summarized data indicated that conception rates increased in mares bred from 48 hours to within 6 hours before ovulation but declined in mares during ovulation and decreased markedly in mares bred 2 to 10 hours after ovulation.¹³ A few mares may conceive if bred or inseminated 6 to 14 hours after ovulation. There is less danger of introducing infection if insemination is performed only once, and at the most twice, during an estrus.

The administration of 2000 to 5000 I.U. of chorionic gonadotropin parenterally on day 2 of estrus usually results in ovulation in the estrous mare within 48 hours and this shortens the estrus and reduces the need for multiple inseminations. One insemination 24 hours after 3,300 I.U. of HCG gave 61 percent pregnancies in one study.³³ Under field conditions insemination every second day is common.

The mare should be suitably restrained. After bandaging the mare's tail with sterile gauze or a bandage, the buttocks, perineal region, and external genitalia are thoroughly scrubbed with mild soap and water, wiped and rinsed with clear water.

Most mares are presently inseminated with a 14 to 16 inch or 35 to 40 cm bovine plastic disposable insemination or uterine infusion pipette attached to a sterile 10 to 40 ml glass or plastic syringe. The tip of the pipette is guided alongside the index finger into and through the

cervix of the mare, which is normally relaxed at estrus. The semen or extended semen is slowly deposited into the body of the uterus. A vaginal speculum and a syringe attached to a long catheter or plastic pipette may be used to inseminate mares but it is more difficult to pass the pipette through the cervix. The cervix and uterus may be injured if too much force is used to insert the pipette or if the mare suddenly moves. Because insemination takes place directly into the uterus, great care is essential to insure that a clean source of semen is used and that a sanitary technique of insemination is followed to prevent genital infections.

In former times semen sometimes was placed in a gelatin capsule. The capsule was held in the hand encased in a disposable glove and sleeve and inserted through the cervix. This is seldom done currently. Another procedure, called "impregnation" was the placement of fresh semen into the uterus of the mare by means of a capsule or inseminating pipette and syringe after its collection from a stallion as he dismounted from the same mare after a service.¹⁶ This has been a long-established custom, done largely because of the wishes of the owners, and also to make certain that the stallion actually ejaculated as determined by microscopic examination of the dismount semen sample for the presence of spermatozoa. There is no evidence that "impregnation" or "capsuling" is of any value and there are several good reasons for not performing this operation. It is one of the most futile things done in the breeding of horses.¹⁵ The last portion of the ejaculate has relatively few spermatozoa; and there is a great risk of introducing infection. There might be a few occasions when "capsuling" or "impregnating" might be indicated, such as a small stallion on a large mare where a "good" cover was not possible.¹⁶

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Artificial Insemination in Horses

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Artificial Insemination in Swine

Application of artificial insemination in swine is highly variable in different regions of the world.^{3,4,20,25,30,32} Substantial numbers of sows and gilts are inseminated in Russia, Hungary, Germany, France, Holland, Norway, Sweden and Denmark.² For example, in Holland and Denmark over 300,000 sows are inseminated (about 20%) and in East Germany 85% of the 1,200,000 sows are inseminated. Most of the semen used is unfrozen. In the United States there is one main supplier of boar semen for artificial insemination. About 20,000 sows are inseminated annually with commercially available semen in addition to boars collected on farms and semen used directly for insemination.

The main advantages of using artificial insemination in swine are similar to those in cattle. The first is the use of genetically superior boars that have been performance and progeny tested for such traits as rate of gain, efficiency of gain, litter size of female progeny, dressing percentage and carcass quality. One boar has the potential of siring up to 1,500 litters per year or 15,000 progeny, although they seldom achieve this potential.

The second advantage of A.I. in swine is disease control. If the boar stud is carefully tested for diseases of importance the semen may be used to introduce new ge-

netic material into specific pathogen-free herds. These include diseases such as virus pig pneumonia, leptospirosis, brucellosis, pseudorabies, tuberculosis, etc. Another advantage of A.I. is the ease with which cross-breeding can be done. A three-breed rotational cross can be used and the owner need only to select females to inseminate with semen from a different breed.

There are several disadvantages of A.I. The first is that the number of sperm cells required and volume of semen used for insemination requires that more boars be kept for the sow population than is necessary in cattle. Secondly, the price of a good boar usually is low enough that swine breeders may find it more economical to buy reasonably good boars and use natural service. Thirdly, as the value of each animal is not high, the cost of insemination may be relatively high compared to the value of the animal. This is especially true where labor costs are high, making the cost per sow expensive. Therefore, most of the inseminations, excepting where the density of pigs is high, are done by farm personnel. It is very important that swine breeders be well trained in heat detection. Thorough training of personnel in detecting estrus accurately is an essential component of a successful A.I. program in any species.

With the present economic climate it is doubtful that A.I. in swine will increase substantially in the U.S., although the use of superior boars can be shown to be profitable. The largest application appears to be either in countries where labor is cheap or herd size is small. With the improvement of conception rates when frozen semen is used it is surprising that more advantage is not taken of the gene pool available through frozen semen. The actual insemination of a sow is easily done and semen can be stored frozen in the same type of liquid nitrogen tank used for bull semen. However, the cost of boar semen is high and fertility results tend to favor natural service.^{7,11,34,38}

Collection of semen from boars for artificial insemination is done by the use of a simple artificial vagina or by the gloved hand grasping the penis¹³ as described in the previous chapter. Young boars are the easiest of the farm animals to train to mount a dummy, especially if other boars have mounted the dummy previously and the urine, smegma and semen odor is present on the dummy. Occasionally young boars may require a gilt or sow in estrus for stimulation. Older boars that have been used in natural service are more difficult to train. Collections are made at 3 to 6 day intervals or 2 to 3 times per week for best results.^{9,20,24,39,40} Some boars can continue to produce satisfactory ejaculates when collected every 48 hours.

Depending on his age and other factors³⁹ a boar will

ejaculate 125 to 500 ml of semen. The presperm fraction, which is usually heavily contaminated with bacteria due to preputial debris and fluid, should be discarded. The extirpation of the preputial diverticulum to reduce the bacterial contamination of semen at the time of collection has been recommended.² This also reduces the boar odor. Douching the sheath and preputial diverticulum and washing the skin around the external preputial orifice will help in reducing the large number of bacterial contaminants in boar semen such as *E. coli*, *Aerobacter* sp., *Proteus*, *Corynebacteria*, *Pseudomonas*, *Staphylococci*, and *Bordetella*. The gelatinous fraction should be discarded during collection or removed by straining through sterile cheese cloth. Either the sperm-rich fraction or the entire ejaculate minus the presperm and gel fractions should be used for insemination.

Using great care to prevent cold shock the semen is examined for concentration, motility and morphology.^{12,18,34} Either a hemocytometer or the photoelectric method⁹ can be used to determine sperm cell concentration in porcine semen. Most authors agree that the numbers of actively motile spermatozoa should be about 65 to 80 percent for best fertility but the relationship between fertility and motility is not high. Fertile boars, especially those in heavy use, may have up to 20 percent or more proximal protoplasmic droplets, but a high percentage of proximal protoplasmic droplets may be associated with infertility. Occasional sterile boars may have a very high percentage of acrosomal defects. Although this defect is usually considered to be hereditary, it might be acquired.²⁰ A typical ejaculate of boar semen would have 200 ml of gel-free volume, 250×10^6 sperm/ml, 70% motile sperm and 15% total sperm cell abnormalities.

Extension of boar semen is based, as in cattle, on the number of actively motile spermatozoa required for optimum conception rates. According to a number of authors³² this varies from 1 to 10 billion actively motile spermatozoa per insemination. Most recommend 5 billion or more. Fairly satisfactory conception rates occurred with 2 to 5 billion per insemination. Thus 10 to 20 sows may be inseminated per ejaculate. During the past several years International Boar Semen, in 10,000 semen collections, has averaged 120 billion sperm per week on a schedule of 2 ejaculates per week. With their recommended dose of 4 billion sperm per week one boar can produce enough semen to inseminate 30 sows per week. Conception rates including size of litters are also influenced by the volume of the extended semen inseminated and the length of storage time before insemination.⁶ Most authors recommend 50 to 100 ml of extended semen per insemination.

Extending boar semen. Boar semen is usually extended from 1 to 1 up to 1 to 8 times, depending on the concentration of motile spermatozoa and the volume of the ejaculate, with warm extender at 37° C immediately after collection. Slow cooling and the addition of phospholipids to the semen protects the sperm cell and aids survival. For use in a liquid semen program the extended semen is cooled gradually to 12 to 20° C (54° to 65° F), which is the optimal storage temperature for boar semen. This temperature requires special packaging for field use. Others cool the ejaculate slowly to 12° to 20° C and then add the extender at the same temperature. When boar semen is cooled to 4° to 5° C within 1 to 2 hours, many sperm cells lose their motility even if extenders have been added. In sperm-rich fractionated semen this harmful effect of cooling is much less pronounced. The addition of egg yolk or milk to boar semen prevented injury to sperm cells at 5° C.⁴ Temperatures of 35° to 38° C are definitely unfavorable to porcine sperm cell survival.

A variety of different types of egg yolk or heated milk extenders have been used to store boar sperm in the liquid state.⁸ Because of the relative difficulty of freezing boar spermatozoa the majority of inseminations are with liquid semen. This semen is useful for up to 3 days of storage.

Frozen boar semen for insemination was given considerable impetus in 1970 when it was reported³³ that a high fertilization rate could be achieved by surgical insemination into the oviducts. For freezing boar semen it is desirable to concentrate the semen by centrifugation in order to have enough sperm cells in a small volume. Several procedures were developed in the early 1970's which produced moderately successful conception rates.^{7,10,15,22,24,26,34,42} In Minnesota^{10,34} the sperm rich fraction was collected and slowly cooled to 22° C. It was determined that exposure to seminal plasma was beneficial to the survival during freezing so the semen was held at 22° C for 1 hour. Thereafter an organic buffer, glucose, sodium citrate, egg yolk and 0.5% of a detergent were added. Semen was cooled to 5° C and pelleted. Considerable attention also was given to thawing.^{8,16,35,36} In the Minnesota studies pellets were initially thawed at 65° C. In Sweden a similar procedure was developed. The final concentration of glycerol was 2.5% (v/v). Sperm were frozen in 0.1 ml pellets. Thawing is done with seminal plasma or other thawing extenders. Thawing media are at 65° C initially but the addition of many pellets results in a final temperature of thawed pellets of about 32 to 34° C.

A series of Beltsville extenders has been developed. One tested widely in the field is BF5.^{11,34} This extender contains Tris, Tes, dextrose, 20% egg yolk and 0.5 per-

cent Orvus Es Paste (a detergent). The semen is held at 22 to 24° C for two hours, centrifuged at $300 \times g$, extended in BF5 to a sperm concentration of 1.2×10^9 sperm/ml. Semen is cooled to 5° C over a period of two hours. Then BF5 containing 2 percent (v/v) of glycerol is added in equal amounts, giving a final sperm concentration of 0.6×10^9 /ml and 1 percent (v/v) glycerol. The semen is then frozen directly by placing 0.1 ml in predrilled dry ice to produce pellets.

It is clear that there are many variations in freezing procedures. All involve certain principles.¹⁰ First, boar semen develops resistance to coldshock by being exposed to seminal plasma. Secondly, seminal plasma is removed before final cooling to concentrate the sperm and cooling must be done slowly. Third, the concentration of electrolytes in the extender should be kept low. Fourth, low glycerol concentrations assist in protecting sperm during freezing, but the glycerol level must be kept low as it is harmful to boar sperm.²³ Finally, by concentrating the sperm the number required for insemination can be frozen in small packages (pellets) for rapid thawing.

Antibiotics should be used to control the large number of bacteria in boar semen stored at near room temperatures.^{29,37,41} Usually 500 to 1,000 I.U. of crystalline penicillin G and 500 to 1,000 micrograms of dihydrostreptomycin per ml of extended semen are recommended. Neomycin, polymyxin B and sulfadiazine are also of value. Improved conception rate and litter size was reported when antibiotics were added to extended boar semen.³² Recently, several of the newer antibiotics such as amikacin and gentamicin have been reported to inhibit bacteria in semen stored at 15° C for many days.³⁷

Detection of estrus and timing of insemination are of critical importance in obtaining good conception rates and litter size in artificial insemination of female swine. Gilts and sows should be observed for estrus twice a day separate from the time of feeding. In this regard the owner's or herdman's and inseminator's judgement, and experience and skills of observation are highly important. Swelling and slight reddening of the vulva in sows and gilts persist for 2 to 3 days of proestrus, 2 to 3 days of estrus and for about 2 days of postestrus, with maximum swelling generally seen at the onset of estrus. The degree of swelling of the vulva alone is unreliable. At the proper time for insemination the vulva is less swollen and more wrinkled and a clear or creamcolored flecked mucus is usually present in the lower vulvar commissure. The gilts and sows often become more restless and noisy during estrus. A method to aid in heat detection consists of approaching the female quietly, placing the flat of the hands on the loins and exerting moderate

downward pressure.¹⁹ If the sow moves away the hands and arms are placed between the hind legs and the rear parts are lifted off the ground, simulating the action of a boar toward a sow in estrus. After a few minutes some sows will stand in a saw-horse attitude (lordosis) when back pressure is applied. If possible the owner, herdman or technician should mount the female and sit astride the loins and remove the feet from the ground. Clawing the shoulders, digital manipulations of the clitoris or inserting the insemination pipette into the vagina will induce the state of sexual receptivity if the sow is in estrus. At this time most sows will stand very quietly and may be nearly insensible to extraneous stimuli. If sows do not show the above signs of estrus, insemination should not be performed as conception rates are apt to be low and litter size reduced due to faulty timing in relation to ovulation. Sows and gilts inseminated during the period of standing reflex, indicating the peak period of estrus, had conception rates of 73 and 61 percent compared to 41 and 46 percent in those sows not showing a good standing reflex.⁷ Sows and gilts should be bred without restraint.

The presence of a boar is very helpful in heat detection. Both the preputial odor of the boar and his vocalizations evoke external behavior signs of estrus in the sow that can be confirmed by hand pressure on the back. A vasectomized boar may be used as a aid in detection of estrus. Also, a boar in a pen adjacent to where the females are being checked for estrus will help evoke signs of estrous behavior.

Lactating sows in good physical condition when weaning their pigs should be watched closely for estrus starting about the third day postweaning. Most sows come into estrus about four to seven days after their pigs are removed. Synchronization of breeding sows can be accomplished by weaning a group of sows at the same time. For best results in insemination of gilts they should not be bred until they have been in estrus twice or more, weigh 280 pounds, or are 8 months of age.

Reports,^{4,24} indicated that the duration of estrus proper averaged 55 hours for gilts and 70 hours for the sow. The time of ovulation was 25 to 36 hours after the onset of estrus. Spermatozoa in the sow retained their fertilizing ability up to 25 to 30 hours. The best time for insemination with unfrozen semen was about 12 hours after the onset of estrus with a second insemination 12 hours later, if the sow or gilt was still in estrus. With frozen semen, it is recommended that gilts be inseminated 16–20 hours after onset of estrus and sows 22 to 26 hours after onset of estrus. A second insemination 12 hours later is recommended. Although under research conditions one well-timed insemination may be sufficient, 2

inseminations under field conditions improve conception rates 15 to 20 percent and litter size by one pig per litter.⁷ This procedure is costly and not necessary if close careful observations and tests for estrus are made.

Three types of insemination catheters and techniques used for inseminating swine have been described.⁸ One type was designed to seal the sow's cervix so no semen flows back into the vagina as the semen is infused. This type is made of rubber about 1.0 to 1.5 cm in diameter and 45 to 50 cm long. The anterior end may be tapered, end in a pear-shaped bulb, or have a corkscrew configuration,²¹ that is pressed with gentle pressure or rotated or twisted counter-clockwise into the cervix. In the latter case the catheter is not easily dislodged. A 7 to 8 mm diameter catheter with an inflatable cuff about 4 to 5 cm posterior to the tip has been devised.¹ The second type of pipette is designed to penetrate through the cervical canal and into the uterus. The diameter of this plastic or nylon tube with a bent tip is 4 mm. It is rotated with gentle pressure to negotiate the cervical canal. The third type is a combination of the two types, consisting of a double plastic tube. The outer tube is 1 cm in diameter and engages in the cervix while the smaller inner catheter is rotated to the left as it is pressed forward from the larger tube. All types of insemination catheters should be inserted dorsal-cranially through the vulva to avoid entering the urethra.

Presently most containers for holding and transporting extended boar semen are plastic bottles and bags that can be attached to the insemination pipette and used to expel the semen. The larger volume of extended semen is squeezed gently over a period of 3 to 5 minutes into the cervix and uterus of the sow. Most workers reported that after a minute or so the semen goes into the sow very rapidly without resistance.

Miscellaneous factors. The results of artificial insemination in swine were more successful in sows than in gilts. Most workers presently report a 50 to 70 percent farrowing rate on first service using single inseminations of fertile semen inseminated correctly at the proper stage of estrus. Conception rates for a single natural services are 80 to 90 percent. With 2 inseminations in one estrus 70 to 80% will conceive.

There are many factors affecting fertility in A.I. Differences among boars is one of the major ones. Frozen sperm are believed not to survive as long in the female reproductive tract. Therefore, timing of the insemination and expert detection of estrus are critical.¹⁴ Finally, the deposition of most sperm into the uterus with minimal loss also is important.

Estrus and ovulation synchronization in swine has been the subject of much research in recent years be-

cause of many desirable features in swine management possible if this could be successfully employed.⁵ The only natural synchronization observed and practiced in swine is that achieved by weaning pigs from sows. Estrus usually follows weaning by 4 to 7 days. One study reported 2 percent of sows were in heat before the fourth day, 12 percent on the fourth day, 35 percent on the fifth day, 16 percent on the sixth day, 16 percent on the seventh day, 6 percent on the eighth day and 13 percent on the ninth to fourteenth day, or 79 percent from 4 to 7 days post-weaning.¹⁹ When young pubertal gilts are transported and placed in a new environment, estrus may develop in up to 70 percent of the gilts within 5 to 10 days due to the induced stress. Early studies on hormonal control of estrus in gilts and sows with gonadotropins, estrogens and progesterone or progestational agents have not been very satisfactory, often because of the production of cystic ovaries.

At one time an excellent synchronizing compound known as I.C.I. 33828 or "Aimax" was available and provided excellent synchronization. However, it was discovered that if this compound was inadvertently administered to pregnant sows early in gestation fetal anomalies were produced. Thus, this compound was hastily withdrawn from the market.

Prostaglandins are not as useful in swine as most other species because the corpora lutea of sows seem only to be susceptible to luteolysis on days 11 to 12 or 14 to 15. One way to overcome this is to administer PMSG or HCG to induce accessory corpora lutea and postpone estrus. Then 12 days later the administration of prostaglandin often will cause regression of the corpora lutea and induce a fertile estrus.

For sows nursing pigs, several can be weaned at the same time after about four weeks of age. Most sows will be in estrus within 2 to 3 days of each other. Then at the other end of pregnancy experimental work with prostaglandin and relaxin may synchronize farrowing so that most pigs can be scheduled to be born Monday through Friday. Further studies are indicated and if synchronization becomes feasible then practical management factors such as the number of boars available for A.I. or natural service, problems of heat detection if A.I. is to be used, the size of the farrowing house, and other factors must be considered.

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Artificial Insemination in Sheep and Goats

In the United States artificial insemination in sheep and goats has not generally passed from the experimental to the practical stage, although technically it has been

feasible for a long time.^{18,23,27,30} Artificial insemination with frozen goat semen has been used in a few goat dairies. In Russia, sheep have been artificially inseminated on a large scale for many years. In Australia, Argentina, Peru, France, East Germany and several countries it has been successfully practiced on a large scale. The advantages and the disadvantages of artificial insemination in sheep are much the same as in cattle. Probably the greatest disadvantages are its high cost when compared to natural service and the difficulties associated with detecting and separating estrous ewes for insemination. With the current success in synchronizing ewes and the development of frozen semen, A.I. could make economical use of the best rams if sheep producers were properly trained to collect semen and inseminate ewes.

It is very important that rams and bucks used for artificial insemination be highly fertile in order to provide the maximum number of inseminations with a high conception rate. Collection of semen by means of an artificial vagina is the preferred method. For rams not trained to the artificial vagina, electroejaculation can provide a satisfactory semen sample.³ Usually a fertile ram or buck can be collected 2 to 6 times or more daily to provide an adequate number of spermatozoa. There is only a moderate decrease in the number of sperm per ejaculate as the ram only ejaculates a limited volume of highly concentrated sperm. A typical ejaculate would contain 0.5 to 1.0 ml of semen with a sperm concentration of about 3 billion cells per ml.

Much of the artificial insemination of ewes is done with freshly collected semen.^{23,25,27,30} Semen should not be chilled if it is to be used immediately. In warm weather (above 20° C) the semen can be allowed to cool to ambient temperature or it can be maintained in warm water at 35° to 37° C. Excellent fertility can be obtained with ram semen used within a few hours as long as sufficient sperm (at least 100×10^6 sperm) are used in well-timed inseminations. This requires only 0.05 to 0.1 ml of normal fresh ram semen to provide this many sperm cells.²¹

If unfrozen semen is to be held for several hours before use,^{19,31} it can be extended at low rates of 1:1 up to 1:10 with heated skimmilk, heated homogenized milk or various combinations of 5 to 20 percent egg yolk with 2.9 percent sodium citrate dihydrate. Sometimes 0.5 to 1.0 percent glucose is added to this solution. Also Tris-yolk extenders, similar to those used for bull spermatozoa, have been used successfully. In glucose-saline buffers best results were obtained with only 1.5% egg yolk or less.³² Storage was at 5° C. When semen is to be stored for several hours it is especially important to use a large number of spermatozoa for insemination. In one study in which 25×10^6 versus 100×10^6 sperm cells were used for insemination fertility had declined

after 5 hours of storage at 5° C, with the greatest decline when only 25 million sperm cells were used. Storage for 48 hours resulted in near zero fertility. However, Salamon²³ compared the fertility of semen extended with a 300 mM Tris, 27.8 mM fructose, 95 mM citric acid plus 14 percent egg yolk when used fresh versus storage for up to 8 days. Then sperm were deposited surgically into the uterine horn. The inseminating dose was 200×10^6 sperm. The percentages of cleaved eggs when semen had been used after 0, 2, 4, 6 and 8 days of storage at 5° C were 95.5, 94.4, 91.3, 75.0 and 52.9. Corresponding samples inseminated normally (into the cervix) after 0, 2 and 4 days of storage at 5° C resulted in 62.5, 40.0 and 0% cleaved eggs. Thus, it is clear that the fertilizing ability of ram sperm can be maintained for many days at 5° C, but the ability for these sperm cells to pass the cervix and be transported to effect normal fertilization is lost rather rapidly during storage.

There has been considerable success with **frozen semen**.^{4,20-23} Again, part of the disappointing results with early frozen semen tests was the greater difficulty in frozen sperm passing the cervix as compared with unfrozen sperm cells. It has been recommended that ewes be tested for the possibility of intrauterine semen deposition via the cervical canal before expensive frozen semen is used. The repeatability of penetration was 0.745.¹³

The extenders used for frozen semen are similar to fresh semen with the addition by glycerol.⁸ Pellets have been found to give good results with raw sperm frozen in a lactose or raffinose extender (166 mM raffinose, 68 mM sodium citrate, 15 percent by volume egg yolk and 5 percent by volume glycerol). After five years of storage at -196° C the lambing rate was 53 percent compared with 54 percent for frozen semen stored for two weeks.²⁸ Maxwell *et al.*²⁰ used a triscitric acid-glucose-egg yolk extender with 6 percent glycerol. Lambing rate with unfrozen semen was 83 percent compared with 55 percent for semen frozen in pellets. In another experiment comparing semen frozen in pellets versus straws the lambing rates were 52 and 29 percent, respectively.

It is apparent that the fertility obtained with A.I. depends upon the extenders used, whether semen is used fresh, cooled and stored or frozen, how it is frozen and thawed,⁴ the number of sperm cells inseminated and the season and fertility of the ewes. Optimal insemination time is 12 to 24 hours after the onset of estrus. With fresh semen 100×10^6 sperm are recommended. With stored or frozen sperm 300×10^6 motile sperm are recommended. If the timing of the insemination is ideal one insemination is sufficient,²⁴ but many studies,¹⁶ particularly in the field result in marked increases in fertility with a double insemination.

The most difficult problem to solve in artificial insemination

ination of sheep is the handling of large numbers of ewes under flock conditions, while still detecting and sorting for breeding the ewes that come into estrus. Rams with aprons, or vasectomized teaser rams may be turned in with the flock of ewes or led through the flock once or twice daily. Vasectomized rams remaining with the ewes can be painted on the brisket or wear jackets holding different colors of paint or chalk to mark the rump of the ewes that are in estrus. Marked ewes are sorted from the flock daily for insemination. This latter procedure has proven most satisfactory for large flocks. Ewes and does in estrus will often bleat, switch their tails rapidly, have an edematous vulva, seek out the ram or buck and stand to be mounted. Does in estrus only occasionally mount each other. Normally estrus lasts about 30 to 36 hours in the ewe and possibly a little longer in the doe. Ovulation occurs late in estrus.

Insemination should take place the last half of estrus. If insemination is to take place only once in a heat period, this should be about 12 to 18 hours after the onset of estrus. Spermatozoa survive about 30 hours in the ewe's genital tract. For insemination the ewe should be placed in a crate that holds her securely and makes examination and insemination easy for the operator. Insemination is accomplished by lubricating and inserting into the ewe's vagina a pyrex glass speculum about 18 cm. (7 inches) long, and 2 cm. (7/8 inch) in diameter. By means of a head light, flashlight, or speculum light the cervix is located and a graduated pipette attached to a syringe is introduced into the cervix and the semen deposited. A speculum with a built in light source is very convenient. Plans and procedures for the artificial insemination of large numbers of sheep have been outlined^{8,12} as management is highly important for saving labor and for good conception rates. It has been demonstrated that if artificial insemination of sheep and goats is carefully conducted during the natural breeding season the results will compare favorably with those produced by natural mating.

Synchronization of estrus has been discussed elsewhere and descriptions can be found.²¹ It is equally important with synchronized ewes to have all conditions optimal, including insemination with at least 200×10^6 sperm.¹⁶ Under proper management conditions ewes can be synchronized and a large number inseminated successfully with semen from high quality rams. Under the usual conditions on farms, natural breeding with good quality rams has been more successful.

Goat A.I. can be carried out in a manner almost identical to sheep. It has one distinct advantage for the owner of a small flock of does with close neighbors. The strong buck odor can be eliminated if the owner desires to use

A.I. to impregnate the does. There are many recent publications on artificial insemination in goats.^{10,11,14,29,30} Results can be very successful. In Norway Fougner^{10,11} reported that buck sperm frozen in Tris-citric acid-yolk extender developed for cattle gave a 63.4 percent conception rate when 3,240 does were inseminated in utero with 75×10^6 sperm. A similar extender has been used in Australia.²⁶ There is a lysolecithin compound in goat seminal plasma which may cause coagulation in egg yolk extenders containing sodium citrate, but this may not be a problem with Tris-buffered egg yolk. Corteel⁶ has eliminated this problem by centrifuging the semen and removing of the seminal plasma. This procedure is generally recommended. He also used milk extender containing 100 gm of skimmed milk powder, 0.194 g. of glucose, antibiotics and 100 ml. of distilled water in the final extender. This extender is heated to 85° C for 10 minutes and cooled. Semen should be extended prior to centrifugation to remove the seminal plasma and then extended again so that there will be 100 million motile sperm per insemination dose. Convenient packages for freezing semen are the 0.5 ml or 0.25 ml French straws manufactured for freezing bull spermatozoa.

For insemination the doe should have the hind quarters elevated over a bale of straw. Or one person can grasp the doe by the hind legs, hold the head down between ones legs and elevate the hind quarters. This provides an ideal position for a second person to insert the semen through the cervix, if possible. The use of a speculum and head lamp is useful in locating the cervix. Experienced inseminators achieve a higher penetration of the cervix and a higher kidding rate (Aamdal).² The insemination should be performed 12 to 24 hours after the onset of estrus.

Does can be synchronized when cycling during the breeding season with progestagens¹⁵ or prostaglandin. The most thoroughly tested method is to insert intravaginal sponges which release a progestagen for 16 days. Administration of 400–600 IU of PMSG at the time of sponge removal brings most animals into estrus within two or three days. A discussion of the various procedures for does both during and outside the breeding season is given by Smith.^{29b}

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Artificial Insemination in Dogs

Artificial insemination is performed most commonly in dogs for reasons that prevent or interfere with copulation.¹³ These include: shyness or fright on the part of either the male or female in the presence of their partner, lack of libido often associated with sexual inexperience in the male or for pathological reasons, including premature erection preventing intromission, phimosis due to a small preputial orifice, painful lesions such as arthritis, spinal lesions, acute prostatitis, and exhaustion especially in obese, young or old, inexperienced dogs on hot humid days. It may also be used for the control of infectious diseases such as caused by *Brucella canis*. The American Kennel Club has not encouraged the practice of artificial insemination, but will allow it to be performed under certain restrictions and stipulations, including the issuance of an affidavit by the sire's owner certifying that he witnessed the collection of semen and the insemination by a licensed veterinarian, and another by the veterinarian certifying that he performed the collection and insemination in the presence of the sire's owner. The male and female dogs are identified and the time and place of insemination is indicated. Relatively

little controlled experimental work has been done with artificial insemination in the dog but the techniques of semen collection and insemination are fairly simple^{1,6,9,10,12,13} and the procedure is often employed by veterinarians.

The favored method of semen collection is by digital manipulation of the penis, with or without the presence of a teaser bitch, to produce ejaculation.^{6,10,12} Semen may also be collected by means of the artificial vagina. A special vagina has been designed with a closed balloon in the space between the liner and casing attached to a bulb which, when squeezed, caused a pulsating pressure on the penis simulating the contractions of the vulva of the bitch.⁹ This artificial vagina could be used with or without a teaser bitch. In contrast to the good results reported with this A.V., another study¹ reported poor motility in the semen collected with the artificial vagina possibly due to overheating of the spermatozoa in the vagina. Digital manipulation is simpler and requires less equipment and produces as good or better semen samples. Dogs may be collected every other day without loss of semen quality. Good quality canine semen should have 70 to 90 percent actively motile sperm cells, less than 10 to 20 percent abnormal cells and a concentration of 90 to 300 million or more spermatozoa per ml, depending upon the amount of prostatic fluid collected.

Semen should be collected in a warm funnel and a 20 ml warmed test tube or a 20 to 30 ml warmed syringe from which the barrel has been removed. Immediately after collection the semen should be placed in warm water at 35° C. if it is not to be used promptly. Undiluted semen, *in vitro*, usually survives about 20 hours. Spermatozoa in extended semen remains viable and capable of fertilizing ova for 4 to 5 days if stored at 5° C. or 40° F.^{9,12} Harrop⁹ preferred heating pasteurized homogenized milk to 92° C. for 10 minutes. The albuminous scum was removed and 500 µg of streptomycin per ml was added. This extender was used at an extension rate of about 1 to 8, with the semen and extender both at either body temperatures, room temperature or refrigerator temperature when added together to avoid cold shock. Foote⁴⁻⁷ reported that the best extender for canine semen was 20 percent egg yolk in a buffer solution composed of 1.45 gm of sodium citrate dihydrate, 0.93 gm of glycine, and 1.25 gm. of glucose per 100 ml of distilled water. The extension rate was 1:10 to 1:20. Each ml of buffered-egg yolk extender contained 1000 units of crystalline penicillin G. and 1 mg of dihydrostreptomycin. This extended liquid semen could be stored at 40° F. or 5° C. for 24 hours before insemination. Good motility was still present after 4 days but no fertility trials were made. Subsequently,⁸ use of the same tris-buffered

egg yolk with glycerol, as is used for cattle, resulted in high pregnancy rates when semen was stored for 24 hours at 5° C. From 100 to 200 × 10⁶ motile sperm per insemination were required. There were no pregnancies with frozen semen. It has been demonstrated that milk extended liquid semen may be shipped over long distances and produce conceptions.⁹

The first successful pregnancies from frozen canine semen was 1969.¹⁷ There have been several reports since that time.^{13,14} Some have used a lactose-egg yolk method devised for pelleting bull semen.¹⁷ Others have used the tris-fructose-citric acid egg yolk extender also developed for bull semen. Semen can be packaged in 0.25 or 0.5 ml straws. After cooling the semen, it can be frozen similar to bull semen. Considerable research still is needed because there is little quantitative evidence of the success rate with frozen canine semen.

Insemination should be performed with undiluted or extended semen 24 to 48 hours after the onset of the estrus. That is the time when the bitch will accept coitus by the dog. A second insemination given one to two days after the first may increase conception rate. Usually at this stage the vulva is still swollen, the vulvar discharge is frequently clear instead of hemorrhagic as in proestrus, and vaginal smears reveal many cornified epithelial cells and few red blood cells. The bitch usually ovulates by the second or third day of estrus, but the ova require several days to mature and shed the polar bodies. Spermatozoa survive 4 to 6 days or more in the female genital tract.² Conception is less likely late in estrus or early in postestrus when many leucocytes are present in the vaginal smear. Vaginal smears may be taken with a cotton swab on a six inch applicator stick, placed on a slide and stained with Wright's or other stain.

A sterile plastic inseminating tube, or pipette, about 20 cm. (8 inches) long and 6 mm. in diameter is fixed to a syringe and the semen is drawn into the syringe. A bovine plastic inseminating pipette broken in half makes a good canine inseminating tube. Most bitches in true estrus stand quietly to be inseminated even though previously they may have resisted normal mating. They should be placed on a table of proper height and held by an assistant. The external genitals are washed and dried. Some veterinarians use a lubricated vaginal speculum and light to locate the cervix, and the insemination tube is placed at or into the cervix where 5 to 10 ml or more of undiluted or extended semen containing about 200 million actively motile spermatozoa should be deposited. Most operators insert the insemination tube without a speculum. In this technique the insemination tube is inserted between the vulvar lips and directed in a dorsal direction until it passes into the vagina. It is then di-

rected horizontally and gently pushed to or into the cervix. It is desirable to elevate the rear parts of the bitch for 3 to 5 minutes after insemination to prevent the possible loss of semen. A finger covered with a sterile finger cot may be inserted into the vagina and the dorsal wall gently stroked or "feathered." This appears to promote the passage of the semen into the uterus. Usually 60 to 80 percent conception rates are realized by artificial insemination with fertile dogs using unfrozen semen. A technique for intrauterine insemination has been described.¹³

Artificial Insemination in Cats

Studies on the reproductive physiology and insemination of cats has been very limited because of their general economic value, and the belief that cats are difficult to handle, especially during mating. Sojka *et al.*¹⁸ described successful procedures for the insemination of cats. Donor toms were selected on the basis of their libido and temperament when a "teaser" queen was placed in the tom's cage. Teaser queens were either normal females in estrus or ovariectomized females that had been given 1.25 mg. **Repositol** diethylstilbesterol subcutaneously every 10 days to produce estrus and acceptance. The selected toms required about 2 weeks of training by a technician to get them to ejaculate routinely into an artificial vagina.

The artificial vagina was made by cutting off the bulb end of a 2 ml rubber bulb-pipet and fitting a 3 × 44 mm test tube into the cut end of the bulb to make a water tight system. The artificial vagina is then placed in a 35 × 75 mm (60 ml) polyethylene bottle filled with water at 52° C. to maintain a temperature of 44 to 46° C. at the time of collection. The rolled end of the rubber bulb-pipet is stretched over the rim of the bottle and the opening of the vagina is sparingly lubricated with K-Y jelly. The artificial vagina is slipped over the penis of the tom as he mounts the teaser female and develops an erection. The technicians other hand is used to steady the tom and queen.

The volume of the ejaculate varied from 0.01 to 0.12 ml, with an average of 0.04 ml.¹⁸ The sperm cell numbers per ml of ejaculate varied from 100 to 5,100 × 10⁶ with an average of 1730 × 10⁶. The total sperm numbers per ejaculate varied from 3 to 143 × 10⁶ with an average of 57 × 10⁶. The motility varied from 35 to 100 percent with an average of about 80 percent. Collection of the semen takes about 1 to 4 minutes with a trained tom. Toms could be collected 3 times a week on a regular basis or daily for short periods and maintain good semen quality. Methods of electroejaculation have been re-

ported.¹⁵ The average volume for 303 ejaculates from 17 toms was 0.23 ml, with a mean of 28 × 10⁶ sperm per ml ejaculate and 60 percent of the sperm being motile. The toms were anesthetized with ketamine hydrochloride (33 mg/kg of bodyweight). Thus, semen collected with the electroejaculator had a higher volume, much lower sperm concentration and fewer sperm per ejaculate, than semen collected with an artificial vagina.

Females bred by artificial insemination can be checked for estrus daily by stroking them on the neck and down the back to the base of the tail and by gently rubbing the perineal region. A queen in estrus will crouch on its sternum, elevate the pelvis, raise and laterally deflect the tail, extend the hind legs, tread with the hind feet and press against the hand when it is held over the pelvic region. Estrus can be confirmed by vaginal smears which contain only large, cornified cells during the height of estrus. Queens are induced ovulators. Queens in full, natural estrus were stimulated to ovulate by the intramuscular injection of 50 I.U. of HCG.¹⁸ The queen was also inseminated at this time by placing 0.1 ml of the saline-diluted semen containing 50 × 10⁶ spermatozoa into the anterior portion of the vagina with a 20 gauge needle, 9 cm long, bulbed at the end with silver solder to make it blunt and attached to a 0.25 ml syringe. A second insemination 24 hours later increased the conception rate.

These authors¹⁸ found that all queens in estrus would ovulate 26 to 27 hours after the injection of HCG. Successful matings occurred up to 49 hours after HCG injection. The queens would accept toms up to 55 hours after the injection. It was also reported that queens in full estrus could be stimulated to ovulate by probing the cervix with a glass rod. This, and the act of artificial insemination at the time the rod or pipette contacted the cervix, often resulted in a characteristic yowl followed immediately by an attempt to lick the perineal region. Thus, the spines on the penis are probably not the cause for this postcoital reaction in the female.

Conception did not occur in queens inseminated with less than 1.25 million spermatozoa. The conception rate was 54 percent (14/26) with 5 to 50 million spermatozoa per insemination. In these insemination experiments¹⁸ the gestation periods ranged from 65 to 72 days, which is nearly a week longer than the 56 to 63 day period that follows natural matings. This should receive further study. Thus, by artificial insemination outstanding toms could be used to breed 12 to 15 queens per ejaculate, compared to natural mating conditions where one tom is usually kept per 15 to 30 females.

There are limited data on freezing feline spermatozoa.¹⁶ Semen was collected 6 months by electroejacu-

lation followed by 6 months with an artificial vagina. The extender was composed of the one used frequently for pellets, containing 20 percent egg yolk by volume, 76 percent of a 11 percent (w/v) solution of lactose and 4 percent by volume of glycerol. Semen was pelleted. Subsequently 56 queens were inseminated in estrus with 50×10^6 or 100×10^6 motile sperm. Six became pregnant, one from semen obtained by electroejaculation and 5 from semen collected with an artificial vagina. Pregnancies lasted 65 to 71 days, with 1 to 4 kittens per litter.

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Other Species

Semen collection and artificial insemination has been reported for many other species.^{2,3} One ruminant of considerable importance in many countries is the buffalo.¹ Many of the techniques developed for cattle are useful in buffaloes. However, libido may be less and there are many problems associated with collection of semen from males and detection of estrus in females. Part of the latter problem is associated with the small group of females and their general management in areas where buffaloes are kept. When A.I. is properly carried out, semen can be preserved and females impregnated successfully.

Artificial insemination has been used by geneticists for multiplying stocks of chickens for decades. This technique is standard practice in the turkey industry where selection for extensive breast meat has resulted in difficulty in natural mating. There are hundreds of references in this field. To date most of the inseminations involve freshly collected semen as fertility declines rapidly with storage. Fertility is reduced by freezing the sperm cells.

Currently, the information on artificial insemination is very fragmentary for most non-domestic species. There is great interest in using this technique to perpetuate endangered species. It has been used quite successfully in several species. One of the problems in mammals, even when semen has been collected and apparently frozen successfully, is to be able to detect estrus in the female. One of the species of great interest which has been reproduced by artificial insemination in China is the great panda. Experiments with this species and many others have been initiated in recent years at several of the large zoos around the world and preliminary success has been reported in the popular press.

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Artificial Insemination in Other Species

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Chapter XX

EMBRYO TRANSFER

By Maarten Drost, DVM*

History

Nearly a century has passed since Sir Walter Heape in 1890 successfully transferred the first fertilized ova between rabbits.²² A number of viable transfers were subsequently reported for laboratory animals such as guinea pigs, mice, rats and rabbits, but it was not until 1932 that Warwick, Berry and Horlacher made the first successful transfers in domestic sheep and goats in the United States.⁴⁰ Then in 1951 Willett, Black, Casida, Stone and Buckner in Wisconsin reported the first successful ovum transfer in cattle using surgical technics.⁴² Rowson and coworkers firmly established the surgical technic as a research tool in cattle, sheep and goats during the 1960's. Rowson and his colleagues were also the first to produce a calf after the 11-day blastocyst had been frozen prior to transfer.⁴³ The introduction of "exotic" (European) breeds into North America in the early 1970's precipitated a major impetus of the application of the technic. By the end of the decade the approach had shifted from surgical to nonsurgical technics in cattle. As with artificial insemination 25 years earlier, embryo transfer has found its widest application, for economic reasons, in cattle.

In livestock the technic of embryo transfer permits the transfer of embryos from genetically superior animals in a population to the less desirable ones. In research, the application of embryo transfer is perhaps limited only by the imagination, and has already provided insight into the causes of early embryonic death, early maternal recognition of pregnancy, maternal-fetal interrelationships and inter-species crosses. The process of embryo transfer is a factorial one whereby each step may limit the number of offspring born, and whereby the end result is the product of the various probabilities involved.

Embryo Transfer in Cattle

Donor Selection

The owner selects his donor animals on the basis of performance and genetic merit, criteria which are gen-

erally more readily available for the older dairy cow than for the beef cow, and preferably would include data for a proven sire she produced. The role of embryo transfer in cattle improvement programs has been reviewed and placed in perspective elsewhere.^{9,24}

Criteria applied by the owner do not automatically make the donor a good prospect for embryo transfer. The donor cow or heifer must be in good body condition and preferably gaining weight. She should be free from underlying disease, a minimum of 50–60 days postpartum and cycling regularly. Generally, cows with a history of reproductive problems do not make good donor animals. Donors are evaluated further by rectal and vaginoscopic examinations. Vaccinations should be current for infectious bovine rhinotracheitis, bovine viral diarrhea, leptospirosis (five types) and clostridial diseases.

Brucellosis and tuberculosis tests should be performed and in the event of export, additional tests for blue tongue virus, leukemia and anaplasmosis. Bloodtyping of the donor for subsequent identification of offspring is required by some breed associations and must be done before embryo transfer. Accurate heat detection methods are also intensified.

Donor Treatment

Single embryos or multiple embryos may be collected from naturally ovulating or superovulated cows respectively. For optimal efficiency 2 to 4 donors should be treated and synchronized with their recipients for each attempt, this allows the sharing of the recommended potential 8 to 10 recipients per donor.

Superovulation remains the least predictable step in the process of embryo production. Tremendous variation in response occurs with age, breed, lactational status, nutritional status, season and stage of the cycle at which treatment is initiated. The most commonly used superovulatory regime for cows in North America involves the use of follicle stimulating hormone (FSH). The short half-life of FSH necessitates twice-daily injections over a period of 4 to 5 days (Table 27). Treatment is begun during the mid-luteal (day 8 to 14) phase of the donor's cycle and employs the use of prostaglandins (PGF2alpha)

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Table 27. Superovulation Treatments in the Cow

Day	Treatment I	Treatment II
-14	donors and recipients	25 mg PGF2alpha
-5	am 5 mg FSH pm 5 mg FSH	7 mg FSH 7 mg FSH
-4	am 5 mg FSH pm 5 mg FSH pm recipients 25 mg PGF2alpha	6 mg FSH 6 mg FSH recipients 25 mg PGF2alpha
-3	am 5 mg FSH am donors 35 mg PGF2alpha pm 5 mg FSH	5 mg FSH donors 35 mg PGF2alpha 5 mg FSH
-2	am 5 mg FSH pm 5 mg FSH	4 mg FSH 4 mg FSH
-1	am 5 mg FSH pm (5 mg FSH)	3 mg FSH (3 mg FSH)
0	Estrus, AI 8 hours after onset of estrus, repeated twice at 12-hour intervals.	

to synchronize the cycles of the donors and the recipients. Alternately, treatment may be initiated on day 16 or 17 (day 0 = estrus) of the donor's estrous cycle. Dose levels of FSH vary from decreasing levels of 7, 6, 5, 4, and 3 mg twice daily²⁶ to increasing levels, or a uniform 5 mg twice daily⁴⁴ injection schedule. Colorado workers¹⁶ reported more ovulations, embryos recovered and pregnancies after a superovulatory regimen with FSH and LH in a 5:1 ratio administered twice daily in decreasing doses for five days. Recent work²⁹ has indicated that an improved response could be obtained when LH was not used. Consequently, two superovulatory regimens with only FSH are used today (Table 27).²⁶ Prostaglandins (PG) (25–35 mg PGF2alpha or 500 mcg PGF-analog (cloprostenol) IM) are routinely given at the time of the fifth and sixth FSH injection which is then followed by estrus and ovulation in 2 and 3 days. This interval from PG to the onset of estrus is 12 to 24 hours shorter in superovulated animals than in naturally ovulating cows. Consequently, recipients should be injected with PGS 12 to 24 hours before the donors if this method of synchronization is used. The response to the foregoing FSH regimens ranges from zero to as many as 50–60 ovulations with an average of 8 to 12. None of the specific dose levels cited has shown a consistent advantage. When a donor has failed to respond to the superovulatory treatment, the second attempt to superovulate her with the same or a

similar regimen is also likely to result in failure. It is difficult to accurately assess the number of ovulations by palpation of the ovaries per rectum when the number exceeds 4 to 6 per ovary or when several anovulatory follicles are present. It is felt that an excessive number of anovulatory follicles in the presence of corpora lutea adversely influences the recovery percentage because of an unfavorable estrogen/progesterone ratio which allegedly affects gamete and embryo transport.

Pregnant Mare Serum Gonadotropin (PMSG) has also been widely used for superovulation. Food and Drug Administration regulations have severely restricted its importation from the traditional South American sources for disease control reasons. While PMSG has the advantage of requiring only a single injection, its half-life is perhaps too long as measurable levels could still be detected in the blood of cows 10 days after the administration of 1500 to 3000 IU PMSG.²⁸ The FSH/LH ratio of PMSG ranges from 1.9 to 95.5 and depends on the stage of gestation at which the serum was collected.²³ PMSG is a crude product and as such is difficult to standardize. It is a foreign protein that is antigenic, which may lead to a reduced response after repeated use.^{5,38} PMSG may be injected SC or IM on day 16 or 17 of a normal estrous cycle. Doses range from 1500 to 3000 IU, but 2000 to 2500 IU are most commonly used. When used in conjunction with PG, PMSG is administered between day 9 to 12 of an estrous cycle followed by PG 48 to 72 hours later. PMSG injections initially exert a luteotropic effect that has been related to its LH activity. LH is presumed to be responsible for the occasional premature ovulation of a large follicle present at the time of the PMSG injection. The precocious CL is believed to inhibit further ovulations, perhaps because it is not old enough to be lysed by PG given 2 days later, yet secretes enough progesterone to block endogenous LH release.

Equine Pituitary Extract and Human Menopausal Gonadotropin are infrequently used. Equine pituitary extract was used successfully to superovulate beef heifers.¹² A single daily injection for three days appeared to be adequate with 75 percent of the cows responding with 5 or more ovulations. In a trial involving 20 cows, Human Menopausal Gonadotropin (equal FSH and LH activities) when compared with FSH was found to be equally effective.¹¹

There is no need to give the donor GnRH or LH at the onset of estrus in an attempt to precipitate or to group ovulations. There is also no benefit from the injection of a physiological dose of estradiol (500 mcg) at the anticipated time of onset of estrus to intensify the expression of heat.¹⁰

Insemination of the Donor

In the presence of hormonally stimulated ovulations, fresh semen gives higher fertilization rates than frozen semen.²⁰ This probably reflects the number of viable spermatozoa in the inseminating dose. Donors should be artificially inseminated 2 to 3 times at 10 to 12 hour intervals beginning 8 to 10 hours after the onset of estrus, to cover the range of time over which the ovulations may occur. Depending on the quality of the frozen semen, it is common practice to use a double inseminating dose at each insemination.

Embryo Recovery

Embryo recovery technics have evolved from slaughter of the donor animals via surgical collection from the anesthetized live animal to nonsurgical embryo recovery from the standing animal. There are several detailed descriptions of the surgical procedures in the literature.^{13,14} The advantages of the surgical approach are that the patient is immobilized, that sterile technic is possible, that the uterus can be manipulated directly, that the ovarian response can be accurately evaluated, that only 20 to 50 ml of recovery medium are needed and that the procedure can be carried out prior to the fifth day after estrus. However, the major disadvantage is the formation of adhesions which limits surgical collections to 1 or 2 operations without lowering reproductive efficiency. The midventral surgical approach further requires operating room facilities and brings with it the risks of general anesthesia. It is difficult in lactating animals with large udders.

Nonsurgical embryo recovery on the other hand is repeatable with relative impunity, it can be performed on the farm, neither fasting nor surgical risk are involved and probably fewer assistants are needed. However, nonsurgical recovery does require considerable manipulative skill and can only be performed in animals in which the cervical canal is passable, and must be done after day 5.

Nonsurgical Embryo Recovery

Bovine embryos descend into the uterus around day 4.5 to 5 (estrus = day 0) and shed their zona pellucida ("hatch") around day 8.5 to 9. Consequently, most nonsurgical recoveries are made between days 6 and 8.

A 2-way or 3-way, roundtip Foley catheter (French size #12-20) with a 30 ml inflatable balloon is used. The 2-way catheter has one channel for inflation of the balloon plus a single channel for alternate inflow and outflow of flushing medium. The 3-way catheter has separate channels for inflow and return flow. A sterile stylet (such as the plunger of an insemination gun) is inserted

the full length of the device to render it sufficiently rigid to allow introduction into the uterus under guidance per rectum. The donor is restrained in a squeeze chute or, in the case of a tractable dairy cow, in a stanchion. The feces are carefully removed from the rectum to avoid aspiration of air, and an estimate is made of the number of ovulations (CL). Inadvertent air can be removed from the rectum with a small stomach tube attached to a "wet-vac" vacuum cleaner. Epidural anesthesia is administered (4 to 6 ml 2 percent lidocaine) to prevent defecation and straining. The vulva and perineal region are thoroughly washed and disinfected with 70 percent alcohol, and the tail is tied out of the way. If the cervix feels small or tortuous, a cervical dilator¹⁴ may be used to gently expand and straighten the cervical canal. The rigid, relatively sharp-pointed dilator should be used with extreme caution as it can readily perforate the uterine wall as it is "forced" through the tight cervical canal. The lips of the vulva are again parted and the Foley catheter, with the stylet in place, is inserted into the vagina and on into the lumen of the expanded cervix. It is then manipulated into the appropriate horn until the inflatable balloon is situated at the base of the uterine horn. The balloon is slowly inflated with 15–25 ml of air in cows and 10–20 ml of air in heifers. The endometrium is easily split by overdistension, resulting in hemorrhage and escape of the flushing solution into the mesometrium from which it cannot be recovered. After the catheter is in position, the stylet is removed and the inlet channel connected by sterile siliconized tubing to a 500 ml bottle of flushing solution. The outlet tubing channels the fluid directly through an embryo filter (75 μ m pore-Em-Con filter) placed well below the level of the uterus. When using the 3-way catheter, the flushing solution flows into the uterus by gravity with the bottle suspended one meter above the level of the uterus. The uterus is manipulated per rectum by alternately lifting and extending the tip of the horn and the intercornual ligament and by compressing the horn or pressing it against the pelvic wall. The out-flow tube may be clamped off periodically to allow build-up of the flushing medium in the uterus. In older cows with long pendulous tracts, manipulation of the cervix and uterus is facilitated by retracting the cervix into the vagina with cervical forceps. The flushing solution usually starts to flow back after 100 to 150 ml have entered the uterus of the cow, or 75 to 100 ml in the heifer. The filter should never be allowed to run completely dry leaving the embryos on the filter dish exposed to the air. A 1 cm layer of fluid can be maintained by manipulation of a clamp on the tubing attached to the bottom of the filter unit.

With the 2-way catheter a 60 ml catheter-tip syringe

may be attached directly to the catheter. The medium is gently introduced and then allowed to flow back into the syringe, if necessary aided by gentle pull on the plunger. This process is repeated 6 to 7 times. Alternately, a Y-connector with inflow and outflow tubes is attached to the 2-way catheter and used in a manner similar to the 3-way catheter by alternately clamping off the outlet and inlet tubing. During the final collection of the flushing solution 50 IU oxytocin may be given IV to aid in the recovery of the last residual portion of the solution. In superovulated cows the procedure is repeated for the opposite horn, using a separate sterile catheter. It is hazardous to re-insert the stylet into the Foley catheter while it is in the uterus because the sharp tip might come out one of the side openings. It is possible to pull the catheter back into the body of the uterus after partially deflating the balloon, until the expanded balloon is held by the cervix. With the catheter stretched by pulling on the extended end, the stylet can be re-inserted until it reaches the tip where it can be palpated. Once the stylet is safely in place, the balloon is deflated and the Foley catheter once again placed one-third of the way into the selected horn. Some operators prefer placement of the catheter with the balloon in the cervix and the tip in the body of the uterus which enables them to flush the horns simultaneously. Immediately after collection, dishes containing media and embryos are placed in an incubator at 39C, but may be kept at 20C without loss of viability. However, fluctuations in temperature must be avoided. Considerable dexterity, patience and practice are needed to achieve consistently satisfactory results.

Flushing Media

The most commonly used medium for nonsurgical embryo recovery is phosphate buffered saline (PBS). A modified solution is prepared by adding 1 percent heat-treated bovine serum^{1,39} and 100 IU sodium penicillin G, 100 mcg dihydrostreptomycin, 0.25 mcg fungizone and 1 mg glucose per ml PBS and .33 mM sodium pyruvate.^{26,41} All culture media are passed through a disposable 0.22 micron millipore filter prior to use. Fetal bovine serum is added at a 20 percent concentration to the flushing medium to make a holding medium. It would seem that the glucose and pyruvate are only necessary for longer term culture of embryos, for "on-farm" use, media need only contain PBS, antibiotics and 1 to 2 percent bovine serum. Bovine serum contains a thermolabile, embryotoxic factor which may be deactivated by heating to 56C for 30 minutes. The serum acts as a protein source for embryo growth and membrane stabilization, and renders the embryos less sticky.

Embryo Handling

Identification and evaluation of embryos is one of the more difficult aspects and requires considerable experience.

The work area must be clean and free from dust. Insecticide sprays should be avoided; some sprays are extremely toxic while the effect of others is unknown. Extreme temperatures are detrimental; stable temperatures are the key to success. The contents of the filter are poured into a (square 100×100 mm) grid searching dish and the filter disk is rinsed completely clean with plain PBS without serum by a forceful stream from a 35 ml syringe and a 22 ga needle. Then 5 to 7 ml of serum is added to the searching dish and stirred while clearing the bubbles from the edge of the dish.

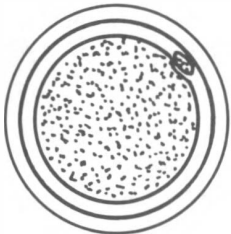
After a brief settling period in the searching dish, the embryos are located as soon as possible so that they may be transferred to sterile holding medium containing 20 percent bovine serum. All dishes must be kept covered between searches to avoid contamination, and particularly evaporation, when placed in the incubator. Evaporation of the small volume of medium in a flat dish rapidly leads to hypertonic solutions.

Embryos are searched for and located at 10–15X magnification and evaluated at 70–100X using transmitting illumination (from below the stage). Embryos are picked up with a sterile, disposable Unipet attached with a short section of rubber tubing to a 0.5 ml syringe, or a shortened sterile tomcat catheter attached to a small syringe, and deposited in a small sterile disposable petri dish (35×10 mm) containing fresh holding medium. In this way the embryos are rinsed and undesirable debris is removed.

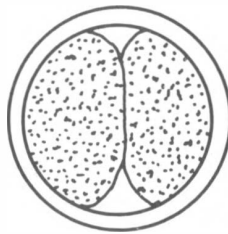
Formerly, recovery rates of embryos were improved by filtration after collection of the large volumes of nonsurgical flushes.³² The technic used a nylon plankton mesh of 56-micron pore size. After filtration was complete, the sieve was backflushed with fresh medium which was subsequently allowed to settle for another 30 minutes before examination.

Morphologic evaluation of embryos is the only practical method to determine the suitability for transfer. Such methods are subjective and depend very much on experience.³⁶ Diagrams of normal embryos at various stages of development are presented in Figure 206. The stage of development after fertilization must be appropriate for the day on which the embryo is collected.

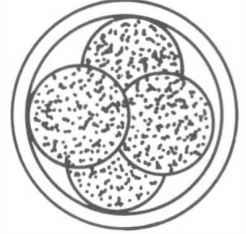
Embryos that are of doubtful quality can be cultured for a few hours. An improvement in appearance will suggest that the embryo is a candidate for transfer. A practical grading system based on morphology places embryos in good, fair and poor categories which pro-



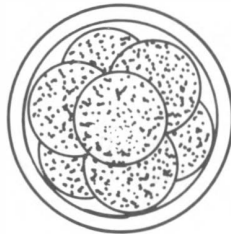
1—cell
Day 0-2



2—cell
Day 1-3



4—cell
Day 2-3



8—cell
Day 3-5



16—cell
Day 4-5



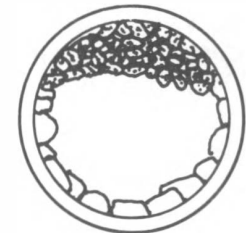
morula
Day 5-6



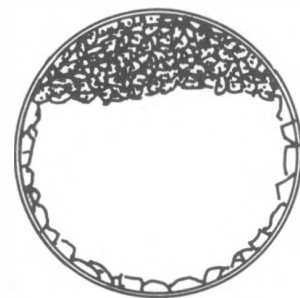
tight morula
Day 5-7



early blastocyst
Day 7-8



blastocyst
Day 7-9



expanded blastocyst
Day 8-10



hatching blastocyst
Day 9-11

Figure 206. Diagrams of Normal Bovine Embryos (adapted from Seidel, G. E. Jr., Seidel, S. M. and Bowen, R. A.^{35b}).

vides a basis for priority of transfer. A good embryo has a regular, round, symmetrical shape in contrast to a fair embryo which shows slight imperfections, an extraneous blastomere or has an odd shape, and a poor embryo which shows severe imperfections. Good embryos resulted in high pregnancy rates (65 percent) while fair and poor embryos resulted in a reduced number of pregnancies (45 and 33 percent respectively).⁴⁴ It is of interest to note that good embryos were less sensitive to exact synchrony between the cycles of the donor and the recipient than fair and poor embryos.

For optimal pregnancy rates, it is advisable to transfer embryos as soon as practical after collection. Enriched PBS allows embryo survival to remain constant for at least 7.5 hours. If embryos are not transferred within two hours from the initial rinse, they should be washed again by the same procedure.

Short-term storage of bovine embryos is possible without significant adverse effects on embryo survival and pregnancy rates whether at 37C for 24 hours³¹ or at 4C for 48 hours.⁶

For long-term storage embryos are frozen to -196C in liquid nitrogen. Mammalian embryos must be stored in a quiescent state to retain viability for a long time. To freeze embryos, a cryoprotectant like dimethylsulfoxide or glycerol is required and slow cooling (0.1 to 2.0C/min) and warming (1 to 50C/min) rates are used. Nucleation or seeding of the freezing medium is a necessity, and stepwise addition and removal of the cryoprotectant at room temperature seems to be beneficial. Using the above parameters, embryos have been frozen and stored at -196C for several years and upon thawing and transfer to a suitable recipient, viable offspring have developed.²⁷

Embryo morphology contributes to the success of the frozen-thawed technics: the presence of the zona pellucida protects³⁷ and the presence of a blastocoele appears to improve survival rates.

Possibly each embryonic stage has its own optimal freezing and thawing requirements.¹⁹ Despite the losses, freezing is used commercially when recipients are not available. Frozen embryos offer a unique advantage for the marketing and distribution of embryos, be it for export purposes or long distance transportation.

Microsurgical technics applied to embryos include removing embryonic cells from, or transferring them into a zona pellucida, biopsy, dividing the embryo in half, aggregating them, injecting nuclei and removing material or structures such as pronuclei. Such manipulations make it possible to analyze chromosomes for sex determination and to produce identical twins or multiplets. Eventually, it may be possible in livestock production to

produce chimeras and homozygous diploid females, to clone by nuclear transplantation and to introduce exogenous genes into pronuclei.³⁵

Recipient Selection and Synchronization

Recipients should be large-framed, healthy, mature heifers or young cows in good condition. A minimum of two normal cycles should have been recorded before use whether they are going to be synchronized with prostaglandins or just selected from a pool of cycling animals. It has been common in embryo transfer programs to overlook the quality of the recipients. Recipients and their maintenance represents the greatest single cost of running a commercial embryo transfer program. Culls from a breeding program, cattle in poor condition and early postpartum animals do not make suitable recipients. Recipients should not be fat and should preferably be gaining 0.1 to 0.2 kg per day. They should be officially calthood vaccinated for brucellosis.

Permanent (double) identification of each animal, meticulous record keeping, accurate heat detection, ample handling and quarantine facilities are all absolute essentials of reliable recipient management. Pregnancy rates are highest when the estrous cycles of the donor and the recipients are synchronized within 24 hours.⁴⁴ Reasonable success can be achieved if they are out of phase by plus or minus one day, but results are too poor to be usable when they differ by two days.

The availability of synchronous recipients can be achieved in three ways: 1) A pool of several hundred cycling females, which limits the number and times when donors can be collected. Five percent of the herd will be in heat on any given day. 2) Large commercial dairy farms can sometimes be persuaded to rent recipients which must of course not be inseminated. A fee will also need to be paid in the event a recipient is not used. 3) A relatively small number of recipients can be synchronized with PG to come in heat the same day as the donor. Animals with a palpable corpus luteum are injected with 25 mg PGF2alpha IM or 0.5 mg PG-analog and may be expected to come into estrus in 2 to 4 days with a peak on the third day. Alternately, all recipients may be injected with PG regardless of the presence or absence of a corpus luteum. The injection is repeated 11 days later and again estrus will peak on the third day after injection. Those recipients which did not respond on the first occasion because they were in the first 5 days of the estrous cycle, respond the second time as they are then in the mid-to-late luteal phase; while the recipients that did respond are in the early-to-mid luteal phase at the time of the second prostaglandin injection.

The average donor yields 7 transferrable embryos. Therefore, 8 recipients per donor is a reasonable number to prepare. When recipients are palpated for corpora lutea, about 20 are palpated in order to definitely identify 12 with corpora lutea on their ovaries. When 12 are injected with PG, 8 on the average will be suitably synchronized with the donor. Recipients must be injected with PG one day earlier than the donor. Due to prior gonadotropin treatment, the donor comes into estrus 48 hours after the PG, while the recipients which did not receive any gonadotropin treatment, will come into estrus three days after PG.

About 85 percent of fertile donors will respond to the superovulatory treatment on the first attempt. For optimal efficiency, 3 to 5 donors should be superovulated at the same time which permits the sharing of the prepared recipients and avoids the expensive failure encountered too frequently when only one donor is prepared at a time.

Transfer

Transfer of bovine embryos may be done either surgically or nonsurgically. The surgical approach seems to produce the most consistent results. Successful nonsurgical transfer requires an even higher degree of dexterity and skill than does the nonsurgical recovery procedure.

Surgical exposure of a uterine horn needs to be done via a midline incision if the recipient is a heifer with a short broad ligament or if she is to receive twin embryos. Halothane anesthesia provides excellent relaxation of the broad ligament. Single transfers are always made to the horn ipsilateral to the corpus luteum: twin embryos should be transferred to separate horns as uterine migration of embryos rarely if ever occurs in the cow. The horn is exteriorized by placing tension on the broad ligament over the distal portion of the horn.

In cows, the incision may be made in the flank on the side of the corpus luteum as far caudally as possible with the animal in the standing position. In both approaches a small stab incision is made along the greater curvature about 7 cm from the tip of the exteriorized uterine horn with a small, closed mosquito forceps. The instrument characteristically "pops" through the endometrium. Care should be taken not to pass through the lumen into the endometrium and submucosa on the other side. The embryo is deposited in the lumen of the uterus via the stab incision with a fine, modified Pasteur pipet. Closure of the abdominal incision following either approach is by routine surgical methods.

Nonsurgical transfers are made through the cervix similar to artificial insemination. It is important to minimize contamination of the uterus because it is more sus-

ceptible to infection during the luteal phase. Feces are evacuated from the rectum and the side of the corpus luteum is determined. Epidural anesthesia is induced to prevent defecation and to minimize straining. The perineal region is thoroughly washed and disinfected with 70 percent alcohol. The embryo is aspirated into a 0.25 ml French straw between two air pockets and two columns of culture medium. The straw is inserted into the AI gun and shortened to fit even with the end of the gun. A gas-sterilized 0.25 ml sheath is fitted over the AI gun and fixed in place. A second, sterile, large sheath which is closed at the distal end is fitted over the first to serve as a cannula and permits passage of the gun through the vagina without coming into contact with the vaginal flora. The tip is placed into the external os of the cervix and is then pushed through the sheath before it is guided as gently as possible through the remainder of the cervical canal and on into the uterine horn on the side of the corpus luteum. The embryo is deposited approximately one-third of the way up the uterine horn and the gun is withdrawn slowly. A negative correlation has been demonstrated between the time spent in the uterine horn and the pregnancy rate.³³ Success is related to dexterity and practice. Pregnancy rates achieved by most operators improve with experience. The pregnancy rate after nonsurgical transfer through the cervix is generally lower than that reported after surgical transfer. In the hands of some experienced embryo transfer practitioners, pregnancy rates following nonsurgical transfer equal those after surgical methods.

Pregnancy rates are higher (approximately 75 percent) after bilateral transfers to non-mated recipients or single transfers to mated recipients. The twinning rate of these recipients is 50 to 60 percent. As a consequence the embryo survival rate percent is not greater.²

Donor and Recipient Aftercare

It is common practice to treat the donor with PG immediately after the collection of ova. At this time the ovaries are generally greatly enlarged by the excessive number of corpora lutea. Such treatment will not only rapidly reduce the size of the ovaries, but also terminate any unwanted pregnancies should an occasional embryo not have been flushed out. It is best not to breed the cow on this induced heat 2 to 4 days later. Furthermore, like a spontaneous heat, the induced heat will have a salutary effect on uterine health should any contamination have been introduced at the time of the collection. Cows can be superovulated at intervals of two months for three treatments without any appreciable decrease in response.¹⁸ Single embryo collections may be made between these superovulatory treatments.

Pregnant recipients should basically be managed like other pregnant cattle. Mature cows should be fed to gain 0.25 kg per day through the seventh month and 0.75 kg per day during the last 2 to 3 months. Heifer recipients should be fed to gain 0.5 to 1.0 kg per day depending on age, size and condition. Overly fat recipients are undesirable. Pregnancy examinations are made at six weeks and confirmed at three months. Pregnancy loss after three months is less than 2 percent. Some recipients will be carrying large fetuses from breeds with a long gestation period and may—particularly when they are heifers—require delivery by cesarean section.

Results Obtainable

The following are average results for several large populations. Superovulation with FSH produces 8 to 12 ovulations per donor.^{18,34} Nonsurgical collections will yield 7 to 10 ova with 75 to 80 percent fertilization rates. Single embryos collected from nonsuperovulated cows tend to result in slightly higher pregnancy rates.^{18,34} Four to seven embryos are suitable for transfer.^{8,18,30,34} Surgical embryo transfer results in a 60 to 70 percent pregnancy rate, while nonsurgical pregnancy rates are 35 to 55 percent, a considerable attrition rate. The range of results varies a great deal from cow to cow; on the average, superovulation and embryo transfer results in four pregnancies per attempt and can be repeated three times per year for an annual total of about 12 offspring.

Cows With Reproductive Problems

Valuable, infertile cows are often presented for embryo transfer. Many of these animals are classical repeat breeders with regular cycles and no palpable abnormalities of the reproductive organs. After a thorough physical examination, nonsurgical embryo transfer techniques may be used for examination of uterine contents and collection of ova. Cases of endometritis not diagnosed by rectal palpation may be obvious when excessive amounts of cellular debris are observed in the sediment of the flushing medium. If aseptic techniques are used the sediment may be submitted for bacterial culture.

Cows with (a history of) cystic follicular degeneration must not be superovulated until after two normal estrous cycles have been observed. After the first observed estrus each problem donor should be subjected to a single ovum recovery to determine: a) the condition of the uterus (nature of the flushing medium); b) if ovum transport is occurring; c) if the ovum was fertilized and d) the stage of development of the embryo.¹⁷ Cows with cystic follicles had fewer corpora lutea after superovulation than cows with uterine infections (4.1 vs 10.1). Furthermore, only 7 percent of the possible ova released (based on the

number of corpora lutea) were fertilized, versus 60 percent in fertile donors. Also, significantly fewer ova and pregnancies per treatment were obtained from cows with cysts than from cows with adhesions.

If an infertile donor does not respond with more than two corpora lutea to either of two superovulatory attempts, it is unlikely that a favorable response will be obtained. Embryo transfer can be used as a refined, sophisticated technic for the diagnosis of infertility.^{3,21,25}

Embryo Transfer in Horses

Oguri and Tsutsumi in Japan reported the first successful nonsurgical recovery of equine eggs as early as 1972 and in 1974 the first successful nonsurgical transfer of 6 to 15 embryos.⁹ Allen and Rowson in England recovered 11 embryos from 30 mares in 1975 and produced 5 pregnancies after nonsurgically transferring 7 embryos.¹

Donor Treatment

The induction of superovulation in the mare has been very difficult. The mechanism of the marked resistance of the ovary of the mare to exogenous gonadotropic stimulation remains unknown. Prospects for induction of multiple ovulations and collection of multiple embryos in the mare have been reviewed.¹⁰

Pregnant mare serum gonadotropin, equine pituitary extracts with,³ and without, human chorionic gonadotropin (HCG)⁶ and porcine follicle stimulating hormone⁵ have all been tried with limited success. Single ovulations can be timed with HCG, 2000 to 3000 IU given intravenously on about the third day of estrus usually induces ovulation 24 to 72 hours later. Natural breeding or artificial insemination are used when ovulation is anticipated from palpation of follicles or following HCG injection.

Embryo Recovery

Surgical recovery techniques were described by Allen and Rowson in 1975,¹ and today are perhaps needed only for small ponies and experimental reasons. Nonsurgical techniques have been adapted from those used for bovine embryos recovery. The easily dilatable cervix and straight uterine horns make the technic of embryo recovery relatively easier than in the cow. Although the embryo arrives in the uterus on day 6, most embryo recovery attempts are not made until 8 or 9 days after ovulation. The large size of the equine blastocyst on day 10 (5–7 mm diameter) precludes transfer of the blastocyst intact.

An extended 2-way Foley catheter (French size 30) is used with simple in-out irrigation. The donor mare is confined in stocks and a thorough prebreeding prepara-

tion is done of the tail, perineum and vulva. The sterile catheter with a stylet in place is introduced per vaginam and passed through the cervix until it is approximately 5 cm into the uterine body. Its position is verified per rectum and the balloon is inflated with 75 ml air after which it is drawn back against the internal os of the cervix to form a seal preventing the escape of the flushing medium from the uterus. One liter of phosphate buffered saline containing 1 percent heat-treated bovine serum is infused into the uterus by gravity flow. Both uterine horns and the uterine body are flushed simultaneously. The return fluid is collected in a prewarmed, sterile, one-liter graduated cylinder or embryo filter placed well below the level of the uterus. The procedure is repeated twice for a total of three liters per collection attempt. Mares predictably return to estrus 3 to 5 days after the flushing procedure in response to the endometrial stimulation.⁷

Synchronization of the Recipients

Close synchrony of the times of ovulation of the donor mare and the recipient mare is desirable for maximal success.⁴

Synchronization of estrus in cycling mares may be achieved by a double prostaglandin treatment. All mares in a group are given a luteolytic dose of a prostaglandin (analog). Mares with a 4- to 13-day old corpus luteum will come into estrus on the third day after treatment and are given 2500 IU HCG IV on the sixth day. Those mares in estrus or with immature corpora lutea at the time of treatment will shortly become diestrous. Fourteen days after the initial injection of prostaglandin all mares are given a second luteolytic dose, and all mares are treated with 2500 IU HCG to synchronize ovulation.

Identification of the Embryo

The collection fluid is allowed to settle for 30 minutes before all but the bottom 100 ml are gently siphoned off, unless an embryo filter has been used. The day 8 post-ovulation blastocyst is 1 to 2 mm in diameter and can frequently be distinguished macroscopically. It can be readily transferred since it is not easily ruptured. Evaluation of its suitability for transfer, like that of bovine embryos, is based on morphological appearance and stage of development in relation to the day of collection. After the embryo is located it is picked up with a fire-polished Pasteur pipet and passed through three consecutive small petri dishes (35×10 mm) each containing a small amount of sterile phosphate buffered saline containing 20 percent heat-treated bovine serum. This procedure washes the embryo by the dilution of possible contaminants. The embryo is stored in a covered dish at 37C until transfer.

Nonsurgical Transfer

The recipient mare is prepared in a manner identical to the preparation of the donor. The embryo is aspirated into a sterile 55 cm insemination pipet in a 5 cm column of medium. The inseminator should wear a plastic palpation sleeve covered by a sterile surgical glove.

The pipet is aligned with the index finger and a second, gas-sterilized sleeve is put on over the pipet. The lips of the vulva are parted and the hand is inserted into the vagina until the index finger has entered the cervix. At this time the pipet is pushed through the outer plastic sleeve and inserted 5 cm into the body of the uterus. Next the embryo is slowly discharged into the uterus. Upon withdrawal of the pipet and the hand from the vagina, the lips of the vulva are held closed to prevent the aspiration of air into the vagina. The pipet is examined for the absence of the embryo by rinsing it with a small amount of medium into a petri dish.⁴ Although surgical transfer has been shown to yield higher pregnancy rates, practicality may dictate the use of nonsurgical techniques. The surgical approaches are analogous to those used in other species and have been well described.⁴

In its research applications, the technic has already contributed much to our understanding of the reproductive physiology and endocrinology of the estrous cycle, early development of the embryo and the early maternal recognition of pregnancy.

The commercial application of embryo transfer will be limited to obtaining offspring from proven infertile mares and the management of older broodmares of the more enlightened breed associations, until the equine industry shows a genuine interest in the propagation of genetically superior animals by relinquishing its restrictions on the use of artificial insemination and embryo transfer.

The meager results obtained in the early 1980's most likely relate to the ability to recover embryos from "problem" mares. At Colorado State University the recovery rate from normal, fertile mares is 70 percent compared to only 26 percent from "problem" mares, mainly due to poor uterine environment or failure of unfertilized ova to pass through the normal uterine tube. If 50 percent of these recovered embryos produce a pregnancy after surgical transfer, the overall chance of success is one foal from eight problem donor mares.

Embryo Transfer in Sheep and Goats

Sheep and goats were the first species of large domestic animals to be used in embryo transfer experiments. Interestingly, the technic was employed to achieve intergeneric and interspecies transfers between goats and sheep.^{9,10} None of the pregnancies endured beyond 55

days probably due to placental differences and diverging endocrine support of pregnancy. In the ewe the CL of pregnancy is no longer needed after 55 days of gestation⁷ while in the goat the CL is required throughout gestation.

Embryo transfer has remained an elegant research technic for the investigation of maternal-fetal interactions.² There has been little if any commercial application in either sheep or goats. In many breeds embryo transfer is limited to the natural breeding season.

Superovulation

The induction of multiple ovulations is principally the same for the (domestic) ruminants. Follicles are stimulated near the end of the luteal phase and early part of the follicular phase of the estrous cycle, be it the natural end or the progestogen- or prostaglandin-manipulated end of the cycle. In the ewe, pregnant mare serum gonadotropin (PMSG) is most commonly used. PMSG is administered IM in a single injection of 1200 IU (range 700–2000 IU) on day 12 or 13 of the cycle, and the ewes may be expected to come into estrus 2 to 4 days later.

Alternately, horse anterior pituitary extracts may be given as three daily doses (total 60 mg) beginning on day 12.⁴ Optimum responses were obtained with horse anterior pituitary extracts in ewes coming into estrus 24 to 48 hours after the end of treatment. The estrous cycle and the time of ovulation can be controlled with the use of either progesterone or prostaglandins which is of value in scheduling the procedure and the recipients.

Progesterone is administered daily by 12 mg per day IM injections or via progestogen-impregnated intravaginal pessaries. Progesterone treatment must be maintained for at least the lifespan of the CL, or 14 days, in the ewe.

Gonadotropin treatment is initiated on the day before the last progesterone injection is given or the day before pessary removal. The ewes generally come into estrus about 2 days after the cessation of progesterone treatment.

Prostaglandins may be given in combination with gonadotropin treatment when the latter has been initiated during the midluteal phase (day 5–10). Prostaglandin (10–15 mg PGF₂alpha or 100 mcg PG-analog) is given 1 to 3 days after the PMSG injection. The majority of the ewes will come into estrus within 36 hours after the administration of prostaglandins.

In the goat, 1000 IU PMSG are given IM on day 17 of the natural cycle. Intravaginal, progestogen sponges may be used to synchronize estrus. The sponges are left in place for 16 to 18 days, or the approximate lifespan of the CL in the doe. PMSG is administered two days

before sponge withdrawal or cessation of daily (12 mg/day) progesterone injections. Equally effective is a dose of prostaglandins (8 mg PGF₂alpha or 50 mcg PG-analog IM) administered between day 6 and 18 of the estrous cycle, two days after PMSG. Porcine pituitary FSH (18 mg in 8 divided doses for 4 days) and horse anterior pituitary extract (40–60 mg in three equal SC injections on consecutive days) have also given satisfactory results of 10 to 16 ovulations.¹

Insemination

The donor animals should be handmated at 12-hour intervals until they no longer accept the male. This approach aids in the timing of estrus and direct observation insures that actual mating took place. Alternately, artificial insemination is also done at 12-hour intervals with the help of a teaser male. An inseminating dose of 400 million or more motile sperm is used at each insemination. Fertilization failure is common in superovulated ewes, particularly in animals showing a high ovulatory response to treatment. This appears to be due to faulty transport of spermatozoa through the cervix and can be overcome by surgical insemination directly into the lumen of the uterus.⁸ The uterine horns are exposed via a midline incision under local anesthesia. Manipulation of the reproductive tract should be kept to a minimum. Fertilization rates in excess of 90 percent of ova recovered, were achieved by injecting 0.02 ml of semen into the tip of each uterine horn around the time of onset of estrus, or on the second day after discontinuing progestogen treatment in synchronized ewes.

In the doe fertilization failure following superovulation is not a severe problem, perhaps because the cervix is more patent in the doe than in the ewe, presenting less of a barrier to sperm transport.⁵

Embryo Recovery

Nonsurgical embryo recovery as described for the cow and the mare is not possible because of the tortuous nature of the cervix and the inability to guide the catheter per rectum. Collections are generally carried out under general anesthesia. This provides maximal relaxation of the broad ligaments and precludes movement of the donor during the procedure. The uterine tubes are cannulated via the infundibulum. A portion or all of the horn and the uterine tube are flushed by gentle expression of the flushing medium from the base of the horns through the uterine tubes.³ Recovery rates of 80 percent can be achieved. Embryos enter the uterus around the third to the fourth day after estrus. Embryos collected on day 3 or earlier (embryos of 8 cells or less) should be transferred to the uterine tubes and yield a 60 percent preg-

nancy rate. Embryos collected on or after day 4 must be transferred to the uterus and will have 70 to 75 percent survival rate.⁵

Luteal failure and early return to estrus occurred in the majority of superovulated does. This resulted in failure to recover embryos later than five days after estrus. By flushing uterine tubes and uteri between day 2 and 4, high embryo recovery rates could be achieved despite the premature luteal failure associated with superovulation in these does.¹ Repeated collections from individual animals have rarely been attempted and would be progressively hampered by the development of adhesions. As in cattle, phosphate buffered media are most commonly used and have the advantage over bicarbonate buffered media in that they do not have to be maintained under a gas phase to maintain pH.

Procedures for embryo handling and evaluation are the same as those already described for cattle.

Recipients

The requirements for synchrony of the cycles of the donor and the recipients in sheep is less exacting than that in cattle. While close synchrony is optimal, a variation of plus or minus two days is adequate in sheep. Critical data are not available for the doe, but there are indications that the doe may tolerate as much as 36 hours asynchrony. If a large pool of recipients is available, animals whose estrus occurs at the same time as that of the donor can be selected. About ten potential recipients should be available for each donor. Prostaglandins or progestogen administration may also be used. Progestogen treatment of the recipients should be discontinued one day earlier than that of the donor. Aftercare of the recipients is the same as that of naturally pregnant females. Nonreturns can be monitored with a teaser male.

Transfer

Transfer via the cervix is extremely difficult in small ruminants because of the tortuous nature of the cervix.⁶ Surgical transfer under local anesthesia via a midventral approach is rapid and economical. Each embryo is transferred with a Pasteur pipet in 0.01 ml of medium to the uterine tube prior to day 4, or to the distal portion of the uterine horn after day 4. Single embryos are transferred to the horn ipsilateral to the CL, twin embryos one to each horn or uterine tube.

Embryo Transfer in Pigs

Genetic progress in the swine industry will require and rely on embryo transfer. There is also considerable interest in the use of embryo transfer to reduce the disease risk involved in the introduction of replacement herd

sires.^{3,4} Embryo transfer has been a useful experimental technic for the study of uterine migration and the spacing of embryos,⁷ the local effect of the embryo on luteal function as well as the effect of a variable number of embryos on the maintenance of pregnancy and embryonic survival rates. Descriptions of embryo recovery procedures have been available since 1962.¹⁰

Donor Selection and Treatment

Sows should be reproductively sound and in good health for optimal results, especially since embryo recovery involves general anesthesia and surgery. Repeated embryo recovery is likely to be limited by adhesions of the uterine horns and ovaries which may have an adverse effect on egg transport and fertilization as well as on manipulation of the reproductive tract.¹²

Superovulation can be induced in sows at weaning by subcutaneous (SC) injection of 1200 IU pregnant mare serum gonadotropin (PMSG) on the day of removal of the pigs.¹⁴ Gilts can be superovulated by the SC injection of 1200 to 1500 IU PMSG on day 15 or 16 of the estrous cycle. Onset of estrus and the time of the LH peak are advanced by about one day, occurring 3.5 to 4.0 days after PMSG treatment in sows. As in other species tremendous variation in the ovulatory response occurs in sows and gilts of similar age, reproductive stage, breeding and management. An average of 20 to 30 ovulations may be expected with a range of 10 to 50.⁶ Donors are mated or inseminated every 12 hours after the onset of estrus. The most important single insemination is at 24 hours after the onset of heat. An inseminating dose of 100 ml diluted fresh semen containing at least 4 billion live spermatozoa is used.

Embryo Recovery and Transfer

Under general inhalation anesthesia, usually maintained by a closed-circuit system,⁸ the reproductive tract is exposed via a midventral incision. Embryos can be collected from the uterine tubes by means of a flared glass cannula inserted at the infundibular end or through the uterotubal junction. Uterine embryos cannot be flushed back through the uterine tubes due to the valve-like nature of the uterotubal junction.

Uterine embryos may be collected by first occluding the uterine horn 25 cm below the uterotubal junction with rubber-shod Doyen intestinal forceps, and then slowly introducing 25 ml of flushing medium into the uterine horn via the uterine tube. Next a cannula (e.g. a 12-French Foley catheter with 5 ml balloon or a flared glass cannula) is inserted through the uterine wall near the uterotubal junction while the fluid is trapped distally by digital pressure. The medium is then allowed to flow

back toward the cannula and an additional 25 ml is infused into the uterus at a point adjacent to the intestinal forceps. Blastocysts, up to day 10 of pregnancy, may also be collected via a catheter inserted through an incision in the isthmus of the uterine tube, through the uterotubal junction and into the uterine lumen. The catheter (ID 1.25 mm) should have two to four sideholes cut in the last 3 cm of the catheter and is inserted into the uterus to facilitate blastocyst recovery.² During the normal rate of development of pig embryos following fertilization,¹¹ cleavage from one to four cells takes place in the uterine tubes during the first 36 hours. They enter the uterus at this stage. Development is generally arrested at the 4-cell stage for up to 48 hours and 4-cell embryos are commonly still recovered as late as 70 to 80 hours after ovulation. When cleavage is resumed, there is roughly a 12-hour cell cycle. However, not all embryos resume cleavage at the same time, hence 4-cell embryos may be recovered in the presence of 8- to 16-cell embryos.¹⁶

Embryo transfer at the 4- to 8-cell stage is recommended primarily because embryos can be evaluated with less difficulty at this stage since normal cleavage is more apparent. A further reason for scheduling embryo transfer in the pig at the earlier stages of development is the sharply reduced embryonic survival rate and pregnancy rate obtained when the transfers are made more than 6 days after ovulation or 7 to 8 days after the onset of estrus.¹¹

The length and tortuosity of the cervix and also of the uterine horns in the pig virtually preclude the possibility of nonsurgical recovery of embryos.

Recipients

Estrus in the recipients should occur within 24 hours of that of the donor, and preferably, the donor should exhibit estrus about 12 hours before the recipient. This may be especially important when sows are used as donors since they tend to ovulate 10 to 12 hours later after the onset of estrus than gilts.⁵ The survival of embryos transferred from sows to already pregnant gilts has been reported.¹ Survival rates for transferred and native embryos were 51 and 35 percent (not significant), 56 and 20 percent ($p < .01$) and 72 and 3 percent ($p < .01$) when the sows were in estrus 12 hours before, at the same time or 12 hours after the recipient gilts.

Weaning may be used to synchronize sows. Prepubertal gilts may be injected SC with 750 IU PMSG followed 96 hours later by 500 IU HCG intramuscularly. The time of HCG injection is then considered as the onset of estrus for the determination of synchrony. The ef-

fective antigonadotropin, synchronizing agent methallibure is no longer available in the U.S.A. because of its teratogenic effects when fed to pregnant sows.

Prostaglandins are impractical in the pig because they are only luteolytic between days 11 or 12 and 14 or 15 in normally cycling animals. Prostaglandins may be used in combination with gonadotropins. PMSG and HCG are used to prolong the luteal phase by inducing accessory corpora lutea (CL) which postpone estrus in all animals. Twelve days after the administration of HCG, prostaglandins can cause all CL to regress resulting in a high degree of synchronization and normal fertility.⁹ A synthetic progestogen, allyl trenbolone or Regumate, shows great promise for estrus synchronization in swine. It is fed for 18 days and, upon withdrawal from feed, estrus occurs 4 to 7 days later with most gilts in estrus on days 5 and 6. Fertility of synchronized gilts was comparable to that for untreated gilts.¹³

Recipient gilts should be examined during surgery to determine that CL of normal appearance are present. Embryos are transferred with a fire-polished Pasteur pipet via a stab incision in the uterine wall about 10 to 15 mm from the tip of the horn. All embryos can be introduced at one site, since spacing within the uterus will occur by intrauterine migration.

Aftercare is routine for a surgical patient. Pregnancy may be diagnosed at 30 to 60 days of gestation with ultrasonic techniques.

Embryo Transfer in Dogs and Cats

The induction of estrus and ovulation in the bitch, and to a lesser extent in the queen, remains an obstacle to the ready application of embryo transfer in these species, although considerable information is available on the endocrinology of the estrous cycle of the bitch^{4,10} and the queen.^{8,9}

Preimplantation canine embryos have been described and illustrated.³ In addition to research applications, the technic of embryo transfer might be used for the genetic improvement of a breed or the preservation of an endangered species with the use of nonendangered and/or domestic canids or felids as recipients.² The difficulty of synchronizing estrus and ovulation of the donor bitch and her recipient(s) might be circumvented by collecting the embryos and freezing them. The embryos could then be transferred to a suitable recipient during her respective natural cycle. However, neither dog nor cat embryos have been successfully frozen and thawed to date. The domestic cat ovulates in response to a coital or hormonal (LH, GnRH) stimulus. Ovulation may be induced by daily

injections of 2.0 mg FSH until estrus is observed at which time she is mated.¹⁰

Embryo Recovery

The donor bitch is anesthetized and the abdomen and perineal region are prepared for surgery. The ovaries, uterus and cervix are exposed via a mid-ventral abdominal incision. The corpora hemorrhagica cannot be observed directly without surgically opening the ovarian bursae, but an impression may be gained by the overall size of the ovary and by direct palpation of the ovary during surgery. A roundtip Foley catheter (8 or 10 French size) made rigid with a stylet is inserted into the vagina. The tip of the catheter is identified at the external cervical os via the abdominal incision and manipulated through the cervix into the lumen of the uterus. The catheter is then directed into a uterine horn 2 cm cranial to the bifurcation. After the stylet is removed, the balloon of the catheter is distended with 3 to 4 ml of flushing medium or air. The ipsilateral uterotubal junction is occluded by digital pressure and a blunt 18-gauge needle is inserted into the lumen of the uterus approximately 4 cm from the uterotubal junction. Next the lumen is flushed with 10 ml of warm phosphate buffered saline solution. The opposite horn is then flushed in a similar manner. Each horn is flushed three times with a total of 30 ml. The flushings are collected via the Foley catheter in sterile petri dishes for examination under a stereomicroscope as described for cattle embryos.¹

In the queen, each horn is flushed separately by introducing recovery medium near the uterotubal junction with a blunt needle and a syringe, and collecting the phosphate buffered saline via a cannula inserted into the lumen near the bifurcation.

Results

Schriver and Kraemer⁵ recovered 47 feline embryos from 9 surgical collections 6 days after mating. Four pregnancies resulted from 9 transfers. Two litters of 3 and 1 males, respectively, were delivered naturally. A third pregnancy resulted in a stillborn male and the fourth pregnancy terminated in either an unobserved abortion or fetal resorption. A total of 72 canine embryos were obtained from 26 collections. Thirty seven of the embryos were transferred to 7 recipients. Three pregnancies were diagnosed and a total of 4 offspring was produced.^{6,7} These studies show that embryo transfer is biologically feasible in the dog and the cat. However, the efficiency must be markedly increased before embryo transfer will be useful in increasing the number of offspring from genetically valuable females, for production

of biomedical models, or for the presentation of endangered species.

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Chapter XIV—Infertility in the Mare

General

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Physiology, Estrous Cycle and Nutrition

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Genital Infection and Pathology

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Chapter XV—Infertility in Sows

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- 1d. Dial, G. D., BeVier, G. W., Hixon, J. E. and Gustafson, B. K. (1984) Endocrine Pathogenesis of Postweaning Anestrus in Swine: Response of the Persistently Anestrous Sow to Hormonal Stimuli, Am. J. Vet. Res. **45**, 9, 1737–1742 (PMSG only hormone capable of inducing a fertile estrus).
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Chapter XVI—Infertility in Ewes and Does

Ewes

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