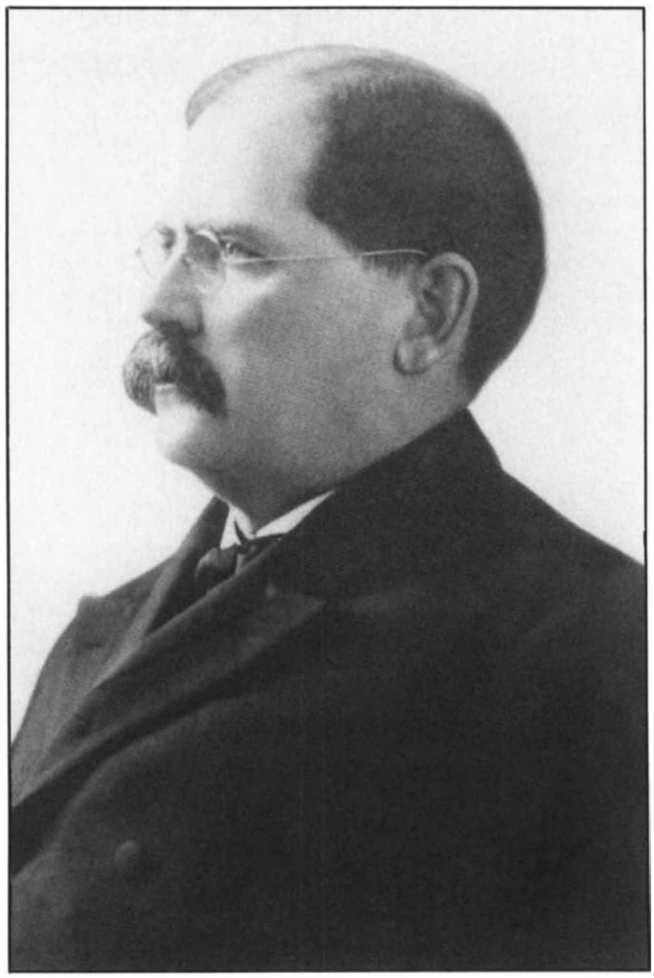

Professor Walter L. Williams
(1856–1944)

Reproductive Pathology of Domestic Mammals

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For Janet, Michael, and Margaret
and in memory of
Peter Olafson

Foreword

This volume reflects the knowledge and wisdom of an experienced and scholarly veterinary scientist. It is based on what a keen observer has seen of natural disease processes, and of those he has induced experimentally; and also on a wide-ranging and comprehensive grasp of the world's literature in the realm of reproductive pathology of animals. To the information derived from these three sources Dr. McEntee has applied four decades of cogitation; his thoughts have often discerned relationships between seemingly disparate aspects of diseases. Such insights have resulted in pathogenetic and/or etiologic discoveries which have helped in the detection, prevention, or treatment of reproductive failures in animals.

Dr. McEntee has brought something more to his studies of reproductive diseases; namely, a point of view, and this, too, is reflected in his book. First of all, he has never been content with mere morphologic descriptions of disease states, but rather has always felt that abnormal function must also be understood, and he has sought whenever possible to contribute to such understanding. Second, to an extent not always found in pathology books, he presents considerable information on the clinical aspects of disease, blending it in an unobtrusive fashion with the pathology so that what emerges is a "seamless" disease entity. Thus while it would be true to say that he is a pathologist's pathologist, it would be only a half-truth. Equally true is that he is also a clinician's pathologist, bringing clinical insights to bear on his approach to disease and pointing out clinico-pathologic correlations, an integration that clinicians appreciate.

The reasons for his approach are several. They begin with a year spent in clinical practice but also include senior academic appointments he has held in veterinary clinics at Cornell University. The third reason is his education by Peter Olafson, who likewise taught pathology not as an esoteric discipline, divorced from practical application, but as the handmaiden of clinical medicine and surgery. McEntee's education can be traced from Olafson back to W. L. Williams at Cornell, an internationally renowned pioneer in reproductive pathology in the first half of this century (see frontispiece). Williams was a prize pupil of William Osler at the Montreal Veterinary College in the previous century. Osler taught what was then a novel doctrine, that pathology was the essential basis of clinical medicine and surgery, both in human and in veterinary medicine.

Dr. McEntee's distinguished professional lineage is not merely of historical interest. In following the Oslerian tradition, he has written a book that will be interesting and useful to the veterinary clinician and the veterinary pathologist alike. Since he deals with the causes of disease, whether infectious, nutritional, toxic, or genetic, the book will interest endocrinologists, geneticists, microbiologists, mycologists, virologists, nutritionists, and toxicologists as well, because it will enable them to orient their own disciplines within the constellation of diseases which affect the reproductive systems.

This book is based on the examination of tissues from over 20,000 cases of reproductive disease in the International Registry of Reproductive Pathology, a unique resource for research, founded by Dr. McEntee at Cornell University and now housed in the Department of Pathobiology at the University of Illinois. The book brings into sharp focus what is known of reproductive pathology, both in North America and abroad. It also indicates clearly what is still not known but needs to be. In these respects it will be of considerable aid as a text and reference book to those attempting to diagnose, prevent, or treat reproductive failures of all kinds. It will also serve as a beacon, lighting up areas where unsolved problems exist for those seeking challenging ones to tackle. The case records, tissures, and photographs in the Registry are available to scholars who are interested in studying them further and can thus extend our knowledge of reproductive pathology.

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Preface

This book evolved from a series of lectures and laboratories on reproductive pathology that I delivered to veterinary students, teachers, researchers, and practitioners at veterinary schools in the United States and at colleges and research institutes in foreign countries. A textbook written in English dealing with reproductive pathology of domestic mammals has not been published previously. While several veterinary pathology books have a few chapters devoted to the subject, many lesions are not discussed. Since this book is intended to serve as a detailed reference source as well as a text, a large number of references are included. The book is intended to help pathologists who are generalists but encounter reproductive lesions on rare occasions as well as those who are specialists but encounter certain diseases only occasionally.

The first chapter is devoted to embryology of the reproductive organs in several species, because knowledge of this subject is essential for the understanding of the pathogenesis of intersexes, gonadal neoplasms, and a variety of other pathologic conditions. There are significant differences between the embryology of the equine gonads and those of the other species of domestic mammals; thus, it is not sufficient to know the embryology of only one species.

One chapter is devoted to normal postpartum involution of the uterus, because normal involutionary changes are often mistaken for pathologic alterations. Other chapters deal with the reproductive organs in the sequence in which they are examined during postmortem inspection; for the female the text starts with ovarian pathology and ends with vulvar lesions, and for the male the material on the testis is presented first and that on the penis last. A discussion of the anatomic features of each reproductive organ of the various species precedes the description of the lesions. This material is presented because all of the normal anatomic features of the reproductive organs of domestic mammals are not described in any single textbook, and a number of normal structures are occasionally misinterpreted as lesions. Thus, it is essential for the veterinary pathologist to be familiar with normal embryology and anatomy before attempting to interpret pathologic alterations.

I am very grateful to the late Dr. Peter Olafson for stimulating my interest in pathology and for providing me with the opportunity to work on reproductive pathology of domestic mammals. The assistance of Drs. William C. Wagner, Donald H. Lein, and Charles C. Hall in conducting necropsies on bulls and cows that provided pathologic material for this book is gratefully acknowledged. The time and effort devoted by Dr. Leon Z. Saunders and Dr. D. Philip Sponenberg to reviewing all of the chapters and to making numerous constructive suggestions are sincerely appreciated. Drs. Susumu Ohno, Robert Habel, and Yang-Dar Yuan reviewed portions of the text. I wish to thank John F. Brock and Samuel Giannavola for preparing the gross photographs, Dr. Robert F. Smith and Professor Donald H. Fritz for the photomicrographs, and Marion Newsom, George Batik, and Donna Lundeen for the drawings. My sincere appreciation is extended to the typing pool at the Veterinary College, Urbana, Illinois, and to Connie Conlon and Eileen Strickland, New York State College of Veterinary Medicine, for typing the manuscript.

Kenneth McEntee

Chapter 1

Embryology of the Reproductive Organs

Testis	**Paramesonephric Ducts and Tubules**
Ovary	**Testicular Descent**
Mesonephric Ducts and Tubules	**Bibliography**

Knowledge of the embryology of the reproductive organs is essential to understand the pathogenesis of many of the abnormal conditions of the gonads and their accessory structures. This knowledge is especially necessary when dealing with intersexes, cystic vestiges of the opposite sex, malformations of tubular reproductive structures, fetal and placental pathology, and gonadal neoplasms. Many of the problems associated with the classification of ovarian neoplasms are due to insufficient knowledge of embryology. The task of the veterinary (comparative) pathologist is complicated because it is necessary to be familiar with the embryology of many species. For example, structure, function, and disease of the equine ovary can be appreciated only when the embryology of the gonad is understood. Its structure and associated pathologic conditions are much different from those of other species of domestic mammals. The equine ovary differs from those of other domestic mammals in that it undergoes very dramatic changes during fetal development, has an ovulation fossa, a central parenchyma corresponding to the cortical tissue of other species, and a very abundant fibrous stroma, and frequently contains ectopic adrenocortical tissue.

"Hamilton, Boyd and Mossman's Human Embryology" (see Hamilton and Mossman, 1972) is recommended for review of the development of the mesonephric (Wolffian) and paramesonephric (Müllerian) systems and Gropp and Ohno (1966) for embryology of the gonads. The gonads originate as thickenings known as gonadal ridges on the medial side of the mesonephros (Wolffian body). The gonadal ridge is a mesenchymal thickening covered by mesothelium. The primordial germ cells migrate from the yolk-sac endoderm to the gonadal ridges. Differentiation of the gonadal ridges begins shortly after the migration of germ cells is completed. Gropp and Ohno (1966) studied the early embryonic development of gonads in cattle by using the alkaline phosphatase reaction. Embryonic bovine gonads present an excellent model for studying the progressive development of the testis and ovary because primordial germ cells, follicular cells in the female, and interstitial cells in the male have a positive alkaline phosphatase reaction. The primordial germ cells lose this activity when they transform to oögonia and oöcytes or spermatogonia.

Gropp and Ohno (1966) concluded that gonadal (sex) cords differentiate, *in situ,* in the gonadal blastema in the central part of the gonadal primordium and that these cords give rise to cortical cords (follicular cell cords) in the female and interstitial cells and tubular structures in the male. The rete testis and rete ovarii also develop from the gonadal blastema. The surface epithelium ("germinal epithelium") does not appear to be involved in the differentiation of gonadal cords. Gropp and Ohno concluded that "Its participation—if any—in the gonadal development is restricted to a very short and rather early period." It is unknown if the early invasion of surface epithelium plays a role in development of the undifferentiated gonadal blastema.

Gropp and Ohno (1966) reported that in 15-mm embryos no sharp separation is present between the coelomic epithelium of the gonadal primordium and the bulk of the gonadal blastema in regard to alkaline phosphatase activity. After a short time, the surface epithelium loses its alkaline phosphatase activity. The undifferentiated gonad then consists of an enzyme-negative peripheral zone, except for germinal cells, and a large positive central zone representing gonadal blastema. Vigier *et al.* (1976) reported the chronology of the differentiation of the reproductive organs of bovine fetuses between 32 and 110 days.

Testis

In the male the germ cells of the outer part of the gonad gradually move into the deeper areas. Alkaline phosphatase-positive strands and negative spots appear in the blastema. The negative spots enlarge and become tubules, lined by sustentacular (Sertoli) precursor cells, which transform into seminiferous tubules. They are surrounded by enzyme-positive interstitial cells. The germ cells then become incorporated into the tubules. At this time germ cells are usually alkaline phosphatase-negative but can be recognized with routine stains by their large size. The germ cells proliferate in the tubules and give rise to spermatogonial precursor cells. The rete testis arises from the blastema. The tunica albuginea develops from mesenchymal tissue directly below the surface epithelium.

Ovary

In the female the alkaline phosphatase-positive germ cells remain in the periphery of the gonad and multiply. Alkaline phosphatase-positive cords develop from the blastema and are separate from the layer of germ cells for a period of time. The cords grow toward the surface and branch peripherally, bringing the cords in contact with the germinal cells. According to Gropp and Ohno (1966), "the cords correspond beyond doubt to the primordia of the follicular or granulosa cell system and should be called follicular cell cords." Oögonia are engulfed by the peripheral branches of the cords and subsequently the germ cells move deeper into the cords. Cords that contain germ cells are called ovigerous cords. The ovigerous cords comprise the cortex below which is a broad intermediate zone containing follicular cell remnants with alkaline phosphatase activity. The medullary cords of the gonadal primordium usually do not contain germ cells and do persist postnatally. They can be a source of tumor formation. The centrally located rete gradually moves from the central part of the gonadal blastema to the hilus.

The ovaries and testes of equine fetuses undergo remarkable enlargement between the third and ninth months of gestation due to hyperplasia and hypertrophy of the interstitial cells (Hay and Allen, 1975). The rapid enlargement of the fetal gonads begins at about 80 to 100 days of gestation and the gonads reach their largest size at approximately 200 days of gestation. The fetal gonads are larger than the maternal ovaries at this time. By Day 250, the fetal gonads are regressing in size owing to degeneration of the interstitial cells.

It has been suggested that pregnant mare serum gonadotropin (PMSG), which reaches maximum levels between approximately Days 50 to 100 of pregnancy, induces hyperplasia and hypertrophy of the interstitial cells in equine fetal gonads. However, the available evidence indicates that PMSG does not cross the placenta in the mare. Wesson and Ginther (1980) presented evidence in favor of fetal pituitary luteinizing hormone (LH) as the cause of enlargement of the equine fetal gonads. They reported that "Fetal pituitary LH concentrations increased between Days 90 to 150 and then remained relatively constant. Fetal blood LH concentrations were highest between Days 100 to 150 of pregnancy during a period of rapid growth of fetal gonads, and the fetal blood LH declined as fetal gonad weights reached a maximum." Fetal pituitary LH concentration increased as fetal blood concentrations decreased. This was interpreted as a possible increase in storage rather than secretion of LH. Samuel *et al.* (1975) found that all pituitary cell types are present in the equine fetus by Day 100 of pregnancy.

The rise and fall of estrogens in the maternal urine closely parallels the increase and decrease in size of the fetal gonads. Raeside *et al.* (1973) presented evidence to indicate that the estrogen production in the pregnant mare depends on the endocrine activity of the fetal gonads. Bilateral fetal gonadectomy resulted in a marked decrease in urinary estrogen, whereas removal of only one fetal gonad resulted in a 50% decrease in urinary estrogens. Equine fetal gonads produce dehydroepiandrosterone, which is an estrogen precursor (Raeside, 1976; Raeside *et al.*, 1979, 1982; Pashen *et al.*, 1982).

Deanesly (1975) reported that "The fetal horse ovary shows an enormous wastage of oöcysts during the meiotic prophase, between Days 73 and 150 of pregnancy. The first groups of oöcysts to enter this phase undergo mass degeneration and eventually disappear; few, if any, oöcysts develop to primordial follicles. Peripheral oögonia, dividing by mitosis, give rise to more oöcysts which pass through the same changes and are also reduced by degeneration, but by Day 150 primordial follicles are fairly common."

When the equine fetal ovary reaches its maximum size at seven to eight months of gestation, it is oval, reddish brown, has a thin cap of gray tissue covering approximately two-thirds of the free border, and weighs 25 to 50 g. The gray tissue contains the ovigerous cords. The rest of the ovary is composed predominantly of hyperplastic interstitial cells, which are large irregular-shaped cells with abundant eosinophilic cytoplasm. Regressive changes commence in advanced pregnancy and continue postnatally. The gray surface area decreases in size to eventually form the ovulation fossa.

Adrenocortical tissue develops in close proximity to the embryonic gonads. In the equine species, nodules of adrenocortical tissue frequently become trapped in the mesovarium (Ono *et al.*, 1969). In the male, nodules of adrenocortical tissue are common in the mediastinum testis, between the head of the epididymis and testis, and in the mesorchium.

The fetal testis secretes at least two hormones that affect development of the reproductive organs. Androgen produced by the interstitial (Leydig) cells masculinizes the mesonephric duct derivatives and external genitalia (Jost *et al.*, 1973). The fetal paramesonephric (Müllerian) inhibitory substance produced by the sustentacular (Sertoli) cells causes regression of the paramesonephric duct system (Josso *et al.*, 1977).

Mesonephric Ducts and Tubules

The urinary and genital systems are closely associated in their embryologic development. Intermediate mesoderm gives rise to a nephrogenic cord and this in turn gives rise to pronephros (cranial segments), mesonephros (intermediate segments), and metanephros (caudal segments). In mammals, the pronephros and mesonephros are temporary excretory organs and the metanephros becomes the permanent kidney.

The genital duct system of the male develops from the mesonephric (Wolffian) ducts and tubules. The efferent ductules of the testis arise from the mesonephric tubules and the epididymis, ductus deferens, ampulla, and vesicular gland (seminal vesicle) from the mesonephric duct. Some of the mesonephric tubules become separated from the mesonephric duct and persist as paradidymis along the course of the epididymis and on the spermatic cord. In young bull calves, they may be observed on the surface of the distal part of the spermatic cord as small, round or oval, flattened, slightly gray bodies. Blom and Christensen (1958) found them in 46% of 267 Red Danish and 25% of 53 Jersey calves.

Paradidymal tissue is difficult to observe grossly in older animals because with increasing age the small bodies become masked by adipose tissue. They are found quite frequently in histologic sections of the spermatic cord and epididymis. They can be recognized most easily on the epididymis by sectioning the body of the epididymis together with the ductus deferens. Paradidymis is frequently present between the two structures. It is composed of glandular ducts lined by a layer of cuboidal to columnar epithelium similar to that of the epididymis. The ducts are surrounded by a thin zone of smooth muscle. Cystic distention of these isolated remnants has not been observed.

In the female, some of the cranial mesonephric ductules (superior aberrant ductules) join the tubules of the rete ovarii. Other cranial mesonephric tubules, together with the associated part of the duct, are blind and form the epoöphoron, which frequently becomes cystic in many species of mammals. Caudal mesonephric tubules become detached from the mesonephric duct to form the paroöphoron, which rarely becomes cystic. Remnants of the mesonephric duct persist along the course of the uterine tubes, uterus, cervix, and vagina to the level of junction with the vestibule of the vagina. These vestiges frequently become cystic.

Paramesonephric Ducts and Tubules

The paramesonephric (Müllerian) ducts give rise to the uterine tubes (oviducts), uterus, cervix, and vagina. The duct begins to develop as an invagination of the coelomic epithelium into the mesenchyme lateral to the mesonephric duct. The opening into the coelomic cavity persists as the abdominal ostium of the uterine tube. The cranial portion of the paramesonephric duct is lateral to the mesonephric duct. The duct crosses the mesonephric duct at the caudal end of the mesonephros and continues to grow in a caudomedial direction to the urogenital sinus.

The paramesonephric ducts fuse to form the uterine body, cervix, and vagina. The caudal end of the vaginal canal may fail partially or completely to open into the vestibule, resulting in a persistent vestige known as the hymen. In heifers, dorsoventral bands of tissue at the junction of the vestibule and vagina are frequently retained and are broken down either by natural service or parturition. A complete hymen is rare in domestic animals but occurs most frequently in the mare.

The embryology of the vaginal epithelium is a controversial subject. The paramesonephric ducts and the urogenital sinus probably both contribute to the development of the vaginal epithelium. Epithelial cells from the urogenital sinus invade the vagina and gradually displace the paramesonephric epithelium for a variable distance depending on the species. In the normal human subject, the vaginal epithelium is considered, by some, to be derived entirely from the urogenital sinus. Vaginal squamous cells, which contain abundant glycogen, are considered to be of urogenital sinus origin. According to Ulfelder and Robboy (1976), in cases of agenesis of the lower part of the human vagina, the proximal segment contains glandular epithelium and glycogen-poor squamous epithelium. They also found similar epithelium in girls exposed prenatally to diethylstilbestrol, indicating that estrogen interfered with complete replacement of the paramesonephric epithelium by the urogenital sinus epithelium. Forsberg (1963) studied the derivation and differentiation of the vaginal epithelium in the rat, hamster, mouse, rabbit, dog, cow, and human female. Special attention was "devoted to the occurrence of degeneration processes, because these are considered essential for the interpretation of possible epithelial displacements." According to Bulmer (1964), the epithelium of the cranial vaginal segment in the ewe appears to be of paramesonephric origin.

Paramesonephric appendages remain on the serosa of the infundibulum of the uterine tube and give rise to cystic structures later in life. These are called accessory funnels (infundibula). The appendix vesiculosa (hydatid of Morgagni) is a cystic accessory uterine tube that develops at the extreme cephalic end of the paramesonephric duct.

In the male, the cranial end of the paramesonephric duct persists as the appendix testis. Remnants of the paramesonephric duct persist along the course of the epididymis, ductus deferens, and ampulla. These remnants frequently become cystic. Cystic remnants at the level of the ampulla are known as uterus masculinus.

Prostate. The prostate develops from endodermal buds from the primitive urethra and the adjacent part of the urogenital sinus.

Bulbourethral Glands. In the male, bulbourethral (Cowper's) glands arise from the penile urethra. Scattered small glands are sometimes present in the penile urethral wall.

Major Vestibular Glands. Major vestibular (Bartholin's) glands develop from the vestibule and are the homologues of the bulbourethral glands. Minor vestibular glands also occur but are usually not visible on gross examination.

External Genitalia. Before sexual differentiation is detectable, a genital (phallic) tubercle and two genital (future scrotal or labial) swellings appear around the cloacal membrane. An endodermal urethral plate develops from cloacal epithelium and extends from the ventral aspect of the phallus to the center and forms the urethra. The urorectal septum divides the endodermal cloaca into the urogenital sinus and rectum.

Testosterone is converted by the enzyme 5-α-reductase to dihydrotestosterone, which induces masculinization of the urogenital sinus and external genitalia. The genital tubercle in the male becomes elongated to form the penis. A urethral groove develops in the urethral plate on the ventral side of the penis. Hypospadias results from the failure of fusion of the urethral folds. The genital swellings fuse to form the scrotum.

In the female, the genital tubercle forms the clitoris and the genital swellings form the labia of the vulva.

Testicular Descent

Wensing (1968) studied descent of the testis in porcine, bovine, and canine fetuses. In 5-week-old pig embryos, the testis is intra-abdominal and connected to the craniomedial pole of the mesonephros. The gubernaculum is a mesenchymal thickening that extends from the caudal pole of the testis to a knoblike expansion between the internal and external oblique muscles at the site of the future inguinal canal. Peritoneum covers the gubernaculum located within the abdomen.

The peritoneum grows into the extra-abdominal part of the gubernaculum to initiate formation of the processus vaginalis. During testicular migration, the total length of the gubernaculum, relative to crown–rump length, remains relatively constant, but the length and bulk of the extra-abdominal part increase considerably as the intra-abdominal part shortens and the testis approaches the internal inguinal ring. The extra-abdominal part grows beyond the external ring to the region of the scrotum. Enlargement of the extra-abdominal part of the gubernaculum is due largely to an increase of extracellular substance, which is strongly metachromatic, indicating a major mucopolysaccharide component. The processus vaginalis follows the outgrowth of the gubernaculum. The cranial part of the gubernaculum enlarges, thus dilating the inguinal canal. The testis then moves rapidly through the canal. As the gubernaculum degenerates, the testis moves into the scrotum. The gubernaculum draws the testis from its original position to the vaginal ring and possibly out through the inguinal canal but not into the depth of the scrotum. There is no organized connection between the tip of the gubernaculum and the scrotal floor.

According to Wensing (1973b), passage of the testis through the inguinal canal of the dog takes place 8 to 10 days after birth. Gier and Marion (1969) reported that inguinal passage of the testis occurs at 100 to 105 days of gestation in cattle, 100 to 110 days of gestation in swine, and during the month before birth in horses.

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Chapter 2

Intersexes

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Bibliography

Diodorus, who lived about 60 B.C., spoke of Hermaphroditus, "who was born of Hermes and Aphrodite, and received the name which was a combination of his parents. Some say that Hermaphroditus is a god . . . has a body which is beautiful and delicate like that of a woman, but has the masculine quality and vigor of a man, but some declare that such creatures of two sexes are monstrosities" (Jones and Scott, 1958). Hermaphrodites occur in all species of domestic mammals but are most common in goats and swine.

Hermaphrodites are classified according to the morphology of the gonads. A true hermaphrodite has one or both gonads containing ovarian and testicular tissue (ovotestis) or has one male and one female gonad. A pseudohermaphrodite has gonads of one sex and accessory reproductive organs of the opposite sex. A male pseudohermaphrodite has testes and female accessory organs, whereas a female pseudohermaphrodite has ovaries and male accessory reproductive organs. Studies of sex ratios, sex chromatin, and karyotypes reveal that the majority of hermaphrodites in most species of domestic mammals are genetic females.

Intersexuality in domestic mammals has been reviewed by Biggers and McFeeley (1966) and Hafez and Jainudeen (1966). According to Biggers and McFeely, "sex is determined at three levels: genetic, gonadal and by the nature of the accessory genital organs. If the sex of at least one level differs from the rest, an intersex results."

Intersexuality

Intersex Goats

The majority of intersex goats are male pseudohermaphrodites with a female karyotype. Eaton and Simmons (1939) reported that 38 (11.1%) of 343 Saanen and 21 (6%) of 350 Toggenburg goats were hermaphrodites. Of 4656 kids in Norway, Haugen (1960) found 234 (5%) to be hermaphrodites. When polled (hornless) does where mated with polled bucks, 7.1% of the offspring were hermaphrodites. None were born from matings of 49 polled does and horned bucks or from 468 matings of horned does with horned bucks. According to Haugen, "Hermaphroditism is hereditary, showing close to 100% linkage to hornlessness, which is hereditary. Hermaphroditism is a recessive character transmitted through heterozygous parents."

The external genitalia of caprine hermaphrodites vary from apparently normal female to apparently normal male. Consequently, the condition is not detectable at an early age in some individuals. Eaton (1943) described a series of 29 cases at 10 days of age, and classified 15 as female type and 14 as male type when judged by external appearance. One goat, which appeared to be a normal female, had ovotestes, aplasia of the uterine tubes, and one uterine horn. Another apparent female had ovotestes and male internal reproductive organs. The other 13 individuals of female type had testes, bulbous vulvas, and varying degrees of enlargement of the clitoris. As the severity of the defect increased, the clitoris projected more prominently from the vulvar cleft and began to resemble a glans penis. All the goats of female type, except the one that appeared to be normal externally, had vesicular glands (seminal vesicles). Of 14 goats with male appearance, 5 appeared to be normal males on external examination. The others had varying degrees of malformation of the penis ranging from a bulbous penile clitoris to a short penis. Hypospadias (Fig. 2.1) was present in four cases. Three were monorchids and the rest had two testes. All the individuals had vesicular glands and 9 of 14 had some degree of uterine development. The external appearance was closely correlated with the degree of development of the internal organs. When the paramesonephric ducts were more strongly developed, the individual appeared externally to be of female type and vice versa.

Hamerton *et al.* (1969) studied 35 polled intersex goats, including 15 Saanens, 3 Toggenburgs, 5 British Alpines, and 12 crossbreeds. Chromosome studies were conducted on 32 goats of which 31 were 60,XX and one was a 60,XX/60,XY mixoploid freemartin. Their anatomical findings were essentially in agreement with those of Eaton (1943). The anogenital distance was used as a quantitative indication of maleness or femaleness in individuals over 20 days of age. They stated that "The normal female anogenital distance is about 2 cm, while in the normal male this distance varies between 30 and 40 cm." Hermaphrodites with an anogenital distance of 2 to 2.5 cm had intra-abdominal gonads, poor development of the mesonephric ducts, and well-developed paramesonephric ducts. Masculinization of both the external and internal reproductive organs was proportional to the anogenital distance. Scrotal or inguinal testes were present when the anogenital distance was 7.0 cm or greater. Three animals had asymmetry of the internal genitalia corresponding with the structure of the gonads. A well-developed epididymis and ductus deferens were present when there was an adjacent testis. A well-developed uterus but a poorly developed ductus deferens and no epididymis was present with an ovary or ovarian tumor.

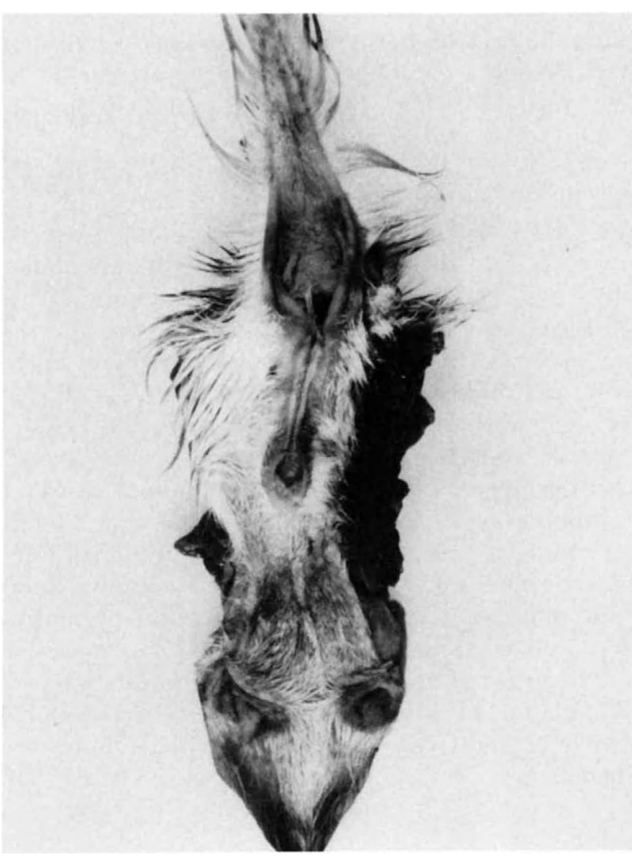

Fig. 2.1. External genitalia of a male pseudohermaphrodite goat with a short penis and hypospadias. Acc. No. 9268.

Hamerton *et al.* (1969) reported that all the gonads had the appearance of testes with the exception of those in three animals that had both ovarian and testicular tissue. One had bilateral ovotestes and the other two had one gonadal tumor (of ovarian or ovariotesticular origin) and one testis. The tumors were not identified with certainty. As an illustration of the uncertainty concerning the diagnosis, three opinions were rendered on one gonad as follows: ovotestis with interstitial cell tumor (hilar cell tumor), ovotestis with granulosa cell tumor, or testis with sustentacular (Sertoli) cell tumor. The "tumors" may have been interstitial gland and sustentacular (Sertoli) cell hyperplasia. The gonads, which were considered to be testes, had seminiferous tubules lined by sustentacular cells but no germinal cells. Two adults had evidence of sustentacular cell hyperplasia. In animals with only testicular tissue, the seminiferous tubules were often atrophied and hyalinized and the interstitial (Leydig) cells were hyperplastic.

McGeady and Fitzpatrick (1978) reported a testicular tumor in a male pseudohermaphrodite goat. The goat had bilateral retained testes and epididymides, well-developed uterine horns, uterine body, a small cervix, vagina, vestibule, and an enlarged clitoris. "A small, encapsulated tumor was found in the right testis. The nature of the tumor was difficult to identify and was probably a Leydig cell tumor."

Basrur and Coubrough (1964) described an intersex polled Saanen goat whose "testicular tissue showed all stages of meiosis and fully formed sperm indicating normal spermatogenesis." Phenotypically the goat was a female, but had a prominent clitoris, a well-developed uterus, and abdominal testes. The uterus contained 950 ml of clear, straw-colored fluid. The goat had a female karyotype.

Wachtel *et al.* (1978) and Shalev *et al.* (1980) found that intersex goats were H-Y^+. H-Y antigen was discovered by Eichwald and Silmser (1955) as a male-specific transplantation antigen in the highly inbred C57BL/6 strain of mice. Skin grafts transplanted from female to male, female to female, and male to male were accepted, whereas transplants from male to female were rejected. The incompatibility of male to female grafts was attributed to a male-specific transplantation antigen determined by a gene on the Y chromosome. Wachtel *et al.* (1975) showed that H-Y antigen is widely conserved phylogenetically. It was found in males of all mammalian species tested, including man. Ohno *et al.* (1976) suggested that H-Y antigen disseminated by gonadal cells entices neighboring cells to engage in testicular organization. Both XX and XY cells possess receptor sites for H-Y antigen.

Shalev *et al.* (1980) reported that "The expression of H-Y antigen by intersex goats was found to be lower than that of normal XY males. The statistical analysis suggests that animals of the same genotype and sex might differ in the density of H-Y antigen on their cell surface, which might explain the variability in primary sex determination among intersex goats."

Hamerton *et al.* (1969) reported that most older intersex animals had pronounced libido in the presence of female goats in estrus. The degree of libido, however, was not directly correlated with the degree of anatomical masculinization. The principal testicular steroid was testosterone and the concentration was often higher in intersex gonads than in normal male testes.

Intersex Swine

According to Pfeffer and Winter (1977), the incidence of hermaphroditism in swine varies from 0.2 to 0.6% in various countries. In certain localities the incidence may be much higher. Baker (1925) reported that in a series of 117 offspring of intersex-producing swine in the New Hebrides, 13 (11.1%) were hermaphrodites. Intersex pigs were selected for use in religious ceremonies.

True hermaphrodites are much more common in swine than in other species of domestic mammals. Albertsen (1951) reported that 81.5% of 233 intersex swine in Denmark were true hermaphrodites. The incidence of intersexes in slaughtered pigs for the years 1933 to 1950 increased from 0.03 to 0.50%. Pfeffer and Winter (1977) found 19 (0.475%) hermaphrodites in a group of 400 pigs slaughtered in Australia. Thirteen (68.4%) of their cases were true hermaphrodites, five were male pseudohermaphrodites, and one was a female pseudohermaphrodite. They reported that ovarian tissue was found only on histologic examination in several cases. In ovotestes, the amount of ovarian tissue was always less than testicular tissue. During a study of intersex pigs in Poland, Bernacki *et al.* (1976) found both ovarian and testicular tissue in 79 (76.6%) of 90 affected animals. Krishnamurthy *et al.* (1971) and Johnston *et al.* (1958) also found true hermaphrodites to be more common than pseudohermaphrodites. Breeuwsma (1969) and Bäckström and Henricson (1971) reported that male pseudohermaphrodites occur more frequently than true hermaphrodites in swine. Pond *et al.* (1961) reported 9 male pseudohermaphrodites and 1 true hermaphrodite in a series of 10 intersex pigs. They were classified as genetic females on the basis of the presence of sex chromatin in the nuclei of liver cells and spinal cord nuclei.

In true hermaphrodite pigs, the left gonad is usually an ovary or ovotestis and the right gonad is usually a testis or ovotestis (Baker, 1926). The ovarian tissue may be functional and result in normal estrual cycles but rarely in pregnancy (Følger, 1932; Petersen, 1952; Hulland, 1964; Cox, 1968; Scofield *et al.*, 1969). Some true hermaphrodites develop follicular cysts. Female pseudohermaphroditism appears to be very rare in swine (Freudenburg and Widmaier, 1959; Pfeffer and Winter, 1977).

The uterus, cervix, vagina, and vulva are usually well developed in intersex pigs. The cervix and vagina may be poorly developed. The clitoris is usually enlarged, and the vulva has a fishhook appearance which is of help in making a clinical diagnosis. Urine tends to be voided in upward spurts. As the intersex pig matures, the uterus frequently becomes filled with fluid. Bäckström and Henricson (1971) cultured the uterine fluid from 21 intersex pigs and isolated bacteria from 14 cases; *Actinomyces pyogenes (Corynebacterium pyogenes)* was the most common organism. I examined one 6-month-old intersex pig that died of peritonitis secondary to pyometra. The uterus contained approximately 5 liters of gray, watery, fetid fluid from which a variety of bacterial organisms were isolated (Fig. 2.2).

The testes of male pseudohermaphrodite pigs are hypoplastic and usually located within the abdominal cavity. In most cases the seminiferous tubules are lined only by sustentacular cells. Baker (1926), Makino *et al.* (1962), and Bäckström and Henricson (1971) reported that germinal cells were present in a few cases.

Bulbourethral, prostate, and vesicular glands may be present. Bäckström and Henricson (1971) reported that male odor is "most evident and significant

Fig. 2.2. Six-month-old male pseudohermaphrodite pig with fluid-filled uterus. Acc. No. 5747. (Figs. 2.2, 2.5, 2.7, 2.9, and 2.18 from Dobberstein *et al.*, 1985.)

when male secondary sexual glands are present." Booth and Polge (1976) investigated C_{19} steroids in testicular tissue and submaxillary glands of five true hermaphrodite pigs between 9 and 15 months of age. They concluded that "the occurrence of C_{19} steroids, including 16-androstenes, in the testicular tissue and submaxillary gland of intersex pigs was of a similar pattern to that in mature boars, and masculinization of the genital tract was related to the amount of testicular tissue." The degree of masculinization of the genital tract was much greater in male pseudohermaphrodites than in true hermaphrodites. High levels of 16-androstenes were found in the submaxillary gland of hermaphrodite pigs, and it was suggested that these steroids are responsible for the "boar taint" in intersex pigs. Hermaphrodite pigs usually exhibit male behavior and mount females in heat.

Intersex Sheep

Hermaphroditism in sheep appears to be rare if male hypospadias is not classified as intersex. A few cases of freemartinism have been reported (Dain, 1971). Dennis (1979) found 3 male pseudohermaphrodites in a series of 401 malformed lambs.

Bruère *et al.* (1969b) described a male pseudohermaphrodite Romney sheep that had only XY sex chromosomes in all tissues studied. It was co-twin to a ewe lamb that was fertile. The male pseudohermaphrodite had a vulva but no clitoris. The vagina was short and blind and no uterine development had occurred. Relatively large testes were located in the abdominal cavity. The epididymides were partially developed and a deferent duct extended from each testis and ended near the midline. No other accessory sex organs were present.

Intersex Horses

Hermaphroditism has been reported much less frequently in horses than in goats and swine. According to Krediet (1939a) a total of 17 cases were recorded in the literature from 1909 to 1938. Many cases of hermaphroditism in horses have been mistakenly diagnosed merely as cryptorchids. With the development of techniques for studying cytogenetics, cases of equine intersexes are being reported more frequently.

Four types of chromosomal abnormalities have been reported in intersex horses (64,XX: Bornstein, 1967; 64,XX/64,XY: Basrur *et al.* 1969; Basrur *et al.*, 1970b; 60,XXXY: Gluhovschi *et al.*, 1970; and 64,XX/65,XXY: Bouters *et al.*, 1972). The case reported by Basrur *et al.* (1969) was considered to be an intersex with unilateral gonadal agenesis. However, the illustration of the left gonad indicates that the cryptorchid castration may have been incomplete and that possibly a gonad was left in the abdominal cavity. In cryptorchid stallions it is not unusual for the body and tail of the epididymis to be loosely attached and relatively distant from the testis. The small cystic structure that Basrur *et al.* (1969) considered to be a gonad appears to be a cystic vestigial duct, possibly of paramesonephric origin.

Krediet (1939a), Senze (1947), Culzoni (1964), McIlwraith *et al.* (1976), and Dunn *et al.* (1981a) have reported cases of true hermaphroditism in horses. Most equine intersexes exhibit male behavior, but some of the true hermaphrodites show female behavior. Krediet (1939b) described an equine case with ovotestes that came into estrus at regular intervals.

The predominant external features of equine intersexes are ventral displacement of the vulva and an enlarged clitoris or short penis. Testes, epididymides, and vesicular glands (seminal vesicles) are usually present, as well as a poorly developed uterus. In true hermaphrodites, the ovarian tissue may consist predominantly of interstitial cells, blood vessels, and fibrous tissue (Fig. 2.3).

Very little has been reported concerning the possible genetic nature of equine hermaphroditism. Levens (1911) reported that 15 intersex foals were sired by the same stallion out of different mares.

XO-gonadal dysgenesis in the mare is described in Chapter 3 under "Ovarian Hypoplasia."

Intersex Dogs

Hare (1976b) reviewed 48 reported cases of spontaneous hermaphroditism in dogs and another 52 known to have been drug-induced. According to his interpretation, 25 were male pseudohermaphrodites,

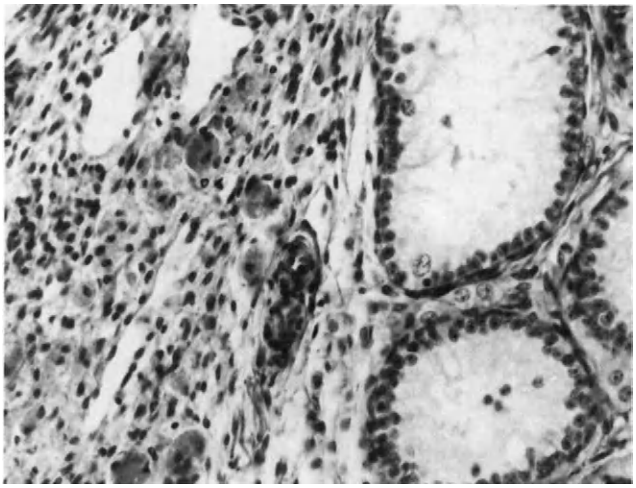

Fig. 2.3. Ovotestis from a 1-year-old equine hermaphrodite. Testis on the right and regressing fetal ovarian tissue on the left. ×204. Acc. No. 14652.

13 were true hermaphrodites, 2 were female pseudohermaphrodites, and 8 could not be classified because of incomplete details in the reports. Fifty-two percent of the dogs had a female karyotype, 38% had a male karyotype, and 10% had a mosaic karyotype. Sixteen of the dogs were Cocker Spaniels and five were Beagles.

Until recently, canine hermaphroditism has been recorded most frequently in Cocker Spaniels. In recent years more cases have been reported in Miniature Schnauzers. The external appearance is feminine in intersex Cocker Spaniels and masculine in intersex Miniature Schnauzers.

The majority of intersex Cocker Spaniels are considered to be females when they are young but their sex becomes doubtful as they mature. Some of the affected dogs assume the male attitude when urinating. Many of the intersex dogs have a large clitoris that may contain an os clitoridis and a rather well-developed uterus. The male pseudohermaphrodites have hypoplastic testes, epididymides, and a well-developed uterus. The testes are frequently retained, but in some cases they descend to the subcutaneous region of the flank.

Seldon *et al.* (1978) studied H-Y antigen expression in a family of American Cocker Spaniels. A true hermaphrodite bitch (78,XX) with bilateral ovotestes gave birth to a litter of three pups. One was a phenotypic and karyotypic female (78,XX), the second (unknown sex) was stillborn, and the third was a 78,XX male pseudohermaphrodite with unilateral cryptorchidism, hypoplastic penis, hypospadias, and a uterus. The XX male pup and his hermaphrodite mother were typed H-Y^+. On the basis of this study, they proposed "that a form of abnormal sexual development, in which individuals with a female karyotype have testes or ovotestes, is caused by anomalous transmission of male-determining H-Y genes."

Intersexual Miniature Schnauzers are phenotypic males that usually have retained testes (Frey *et al.*, 1965; Norrdin and Baum, 1970; Brown *et al.*, 1976). Cytogenetic studies have revealed that male pseudohermaphrodite Miniature Schnauzers are genetic males (Chaffaux *et al.*, 1980; Marshall *et al.*, 1982). Most reported cases were not recognized as intersexes until surgery was performed to remove neoplastic gonads. The predominant testicular tumor in all cases was of sustentacular cell origin. Seminomas and/or interstitial cell neoplasms have also been found. The latter neoplasms are usually smaller than the sustentacular cell neoplasms and may be overlooked if multiple tissue sections are not prepared. In addition to testes, the male pseudohermaphroditic Miniature Schnauzers have epididymides, ductus deferentes, prostate, penis, and uterus. Clinical signs of hyperestrogenism, including attraction of male dogs, alopecia, and gynecomastia, are associated with the presence of a functional sustentacular cell tumor. The uterus undergoes cystic hyperplasia of the estrogenic type, resulting in mucometra (Fig. 2.4) and occasionally pyometra.

According to Jackson *et al.* (1978), "Neurogenic incontinence appears to be a common finding in canine pseudohermaphroditism associated with abnormalities of the vagina or urethra (or both)." They reviewed the literature on the association between hermaphroditism and incontinence and presented a case in a 1-year-old Pekingese × Poodle with female pseudohermaphroditism. The dog was presented for examination because of urinary incontinence of at least five months' duration. It squatted in female fashion to

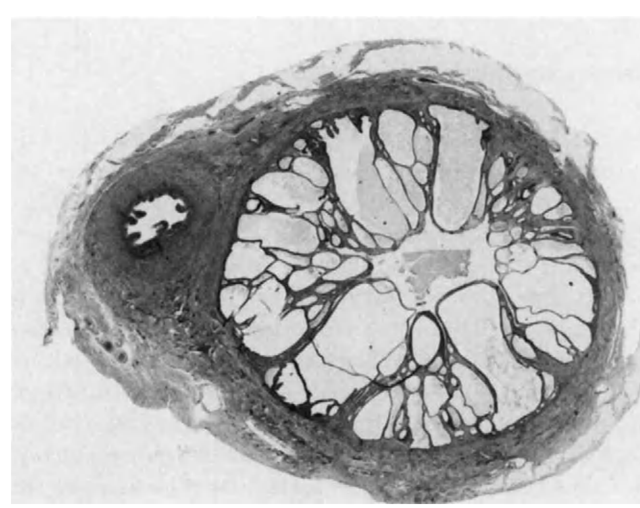

Fig. 2.4. Uterus and ductus deferens from a 10-year-old male pseudohermaphrodite Miniature Schnauzer dog with cystic hyperplasia of the endometrium. ×11. Acc. No. 18739.

urinate and dribbled urine while standing or lying. The condition was alleviated by ovariohysterectomy and surgical correction of the urethrovaginal fistula but the dog subsequently developed estrogen-responsive urinary incontinence. Female pseudohermaphrodite dogs frequently develop urovagina (urinary stasis in the proximal vagina).

In addition to the case of female pseudohermaphroditism reported by Jackson *et al.* (1978), other cases have been recorded by McFeeley and Biggers (1965), Hoffman (1972), Rothuizen *et al.* (1978), and Weaver *et al.* (1979). Female pseudohermaphrodites have a penis and prepuce, which are usually underdeveloped, and have normal female internal reproductive organs with functional ovaries.

Hermaphroditism in dogs appears to be genetic but the mode of inheritance has not been determined (Hare *et al.*, 1974). Stewart *et al.* (1972) were not able to determine the mode of inheritance of three cases of hermaphroditism that appeared to be hereditary in a group of Pug dogs.

Intersex Cats

The tortoiseshell male cat is rare and usually sterile because of testicular hypoplasia. The condition in the cat and other species with XXY sex chromosome constitution (Klinefelter's syndrome) is discussed in Chapter 13 under "Testicular Anomalies."

Hermaphroditism in the cat appears to be extremely rare. Biggers and McFeeley (1966) quoted H. C. Thuline and D. E. Norby (personal communication) as having described a true hermaphrodite cat with an XX/XY mosaic karyotype. Harman (1917) reported a true hermaphrodite cat in which the left gonad was a testis and the right gonad an ovotestis. The left testis had descended through the inguinal canal and the right ovotestis was located caudal to the kidney. There was a uterine tube and uterine horn on the right and spermatic cord and ductus deferens on the left. A prostate was present but bulbourethral glands and epididymides were not mentioned.

Diegman *et al.* (1978) recorded a case of female pseudohermaphroditism in a Siamese cat that exhibited female behavior but had a well-developed penis and prepuce. It had normal-appearing ovaries and uterus. The histology of the gonads and the karyotype were not reported.

Herron and Boehringer (1975) reported a case of male pseudohermaphroditism in 1-year-old, blue tabby cat that was considered to be a normal female. During ovariohysterectomy the gonads were noticed to be unusually large. The uterus appeared to be normal. Histologic examination revealed that the gonads consisted of seminiferous tubules lined merely by sustentacular cells with islands of interstitial cells between the tubules. Each gonad had an associated epididymis and ductus deferens. The uterus appeared normal with an inactive endometrium. The cat was considered to be a genetic male, because Barr bodies (Barr *et al.*, 1950) were not found during the examination of 400 cells from the oral mucosa. The presence of a Barr body in the nucleus of a cell indicates that the cell contains two X chromosomes. Since the male has only one X chromosome, Barr bodies are not present in the nuclei of their cells.

Intersex Cattle

Intersex cattle, other than freemartins, are comparatively rare. A few cases of male pseudohermaphroditism in cattle have been reported. True hermaphrodites are rare and female pseudohermaphrodites are extremely rare (Fig. 2.5).

McFeeley *et al.* (1967) recorded the karyotypes of four bovine male pseudohermaphrodites. They reported that one was karyotypically male, two were XX/XY chimeras, and the fourth was recorded as XX/X?. Dunn *et al.* (1970) reported an unusual case of a bovine true hermaphrodite with a diploid XX/triploid XXY chimerism: "Only XX diploid or near diploid cells were seen in the first 300 metaphases from cultured peripheral blood, but a single 88,XXY metaphase was found when an additional 400 metaphases were scored." This article emphasizes the danger of scoring a limited number of metaphases when studying intersex individuals. It is also one of the few reports demonstrating postnatal survival in diploid–triploid chimeric animals.

Brogger and Aagenaes (1965) reported that "sex chromosome mosaicism is important in the etiology of true hermaphroditism, and that such mosaicism may be more common in true hermaphroditism than hitherto recognized." Dunn *et al.* (1968a) recorded a case of XX/XY chimerism in a bovine true hermaphrodite. They suggested "three possible mechanisms for sex chromosome chimerism: (1) intrauterine exchange of cells between heterosexual twins with anastomosed chorionic vessels, (2) early mitotic errors in an XY zygote and (3) dispermic fertilization of an ovum and its polar body, or two ova, with subsequent fusion."

Kieffer and Sorensen (1971) studied three bovine intersexes. One was born co-twin to a bull and the other two were singletons. The twin had subcutaneously located testes and a urogenital opening located about 30 cm below the rectum. All the male accessory sex glands were present but no development of female reproductive organs was evident. The chromosome composition of the peripheral blood was found to be 60,XX as determined by examination of 200 metaphases. It is possible that XY cells might have

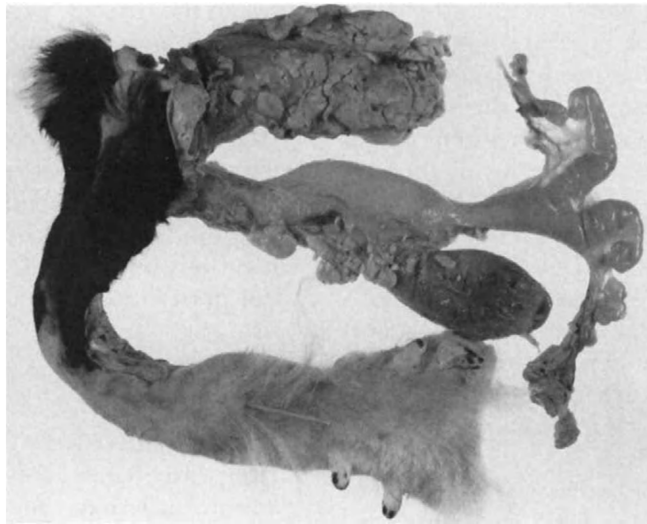

Fig. 2.5. Female pseudohermaphrodite heifer with ventrally displaced vulva. Applicator stick in vulvar opening. Acc. No. 4018.

been found had more cells been counted. The single-born intersexes were true hermaphrodites. One had a well-developed uterus, atresia of the caudal part of the vagina, and the external opening of the urogenital tract was located slightly caudal to the teats. The other true hermaphrodite had a blind uterine horn on the right side along with an ovotestis and a vesicular gland (seminal vesicle). Testis, epididymis, and ductus deferens were located on the left side. The urethra opened between the rear legs. XX and XY cells were found in the peripheral blood of both true hermaphrodites.

Fürst (1952) described a 2 1/2-year-old, pregnant, bovine, true hermaphrodite. One gonad was an ovary and the other a hypoplastic testis. The fetus was in the uterine horn on the side containing the testis.

Freemartinism

Freemartin Cattle

Freemartins are XX/XY chimeras that develop as a consequence of fusion of the chorioallantoic circulation in pregnancies consisting of at least one male and one female fetus. In cattle, approximately 92% of female calves born co-twin with males are freemartins. A few cases of freemartinism have been reported in sheep, goats, and swine.

The literature on the freemartin condition has been reviewed by Swett *et al.* (1940), Bertrand (1965), and Marcum (1974). The freemartin was known to cattle breeders before the establishment of the Roman Empire. Swett *et al.* (1940) reported "the sterile cow born twin to a bull was referred to by Varo, a writer who died in 28 B.C. It is called 'taura,' which apparently meant barren cow." Forbes (1946) searched for the origin of the term freemartin but could not fully establish the etymology. He offered the hypothesis "that 'freemartin' may have signified an 'ox-like or bull-like' cow, just as 'taura' may have indicated female bull." According to Short (1969), "the prefix 'free' meant 'barren,' or alternatively 'bull or ox-like' and 'mart' or 'martin' was a cow, ox or spayed heifer killed at Martinmas (11 November), when the meat would be either dried, salted or smoked for storage through the winter."

The freemartin condition develops in a female fetus when the chorioallantoic circulation is fused, allowing interchange of blood between heterosexual twins. Keller and Tandler (1916) and Lillie (1916, 1917) theorized that masculinization of the female fetus is induced by hormones from the developing testes of the male twin. However, freemartinism does not occur when androgens are injected, early in pregnancy, into cows carrying female fetuses (Mason *et al.*, 1958; Jost *et al.*, 1963; Jainudeen and Hafez, 1965). This treatment induces masculinization of the external genitalia but does not alter development of the ovaries or uterus.

Herschler and Fechheimer (1967) proposed that the freemartin condition is due to the presence of XY cells in the circulation. Vigier *et al.* (1977) reported that XX/XY chimerism is not the cause of the early changes in the female fetus. They demonstrated that "by surgically separating twins on Day 37 and 45, i.e., after vascular anastomoses and chimaerism had been established; the female twins had XY cells in the liver but showed no sexual anomalies on Day 60."

Androgen appears to be responsible for the development of male accessory reproductive organs and anti-Müllerian (paramesonephric) hormone for suppression of the development of female accessory organs in freemartins. Masculinization of the freemartin gonad appears to be due, at least in part, to the presence of H-Y antigen produced by the male twin.

Ohno *et al.* (1976) reported that the H-Y antigen in the bovine freemartin gonad plays a hormonelike role. It was proposed that the "H-Y antigen disseminated by XY gonadal cells entices neighboring XX cells to engage in testicular organization." Wachtel *et al.* (1980) stated that "we believe that Lillie's humoral theory is vindicated, for we now have clear evidence that H-Y is disseminated in the male, transmitted in the serum and bound by gonad-specific receptors of the female."

The external appearance of a freemartin may vary from an apparently normal female to a somewhat masculinized individual. The vulva may be small and ventrally displaced with long, coarse hair extending from the ventral commissure (Fig. 2.6). The clitoris is frequently, but not always, enlarged and if greatly enlarged may cause urine to spurt upward when the animal urinates. Buyse (1936) reported "the presence of a penis-like organ, 26 cm in length," in the vestibule of the vagina in a Brown Swiss freemartin.

The internal reproductive organs of freemartins are characterized by masculinization of the gonads, retarded development of the paramesonephric (Müllerian) duct derivatives, and development of the mesonephric (Wolffian) duct derivatives (Fig. 2.7). Chapin (1917) compared the histology of the genital organs of bovine fetal freemartins with those of normal male and female fetuses of the same approximate size. The length of the fetuses ranged from 7.5 to 29.5 cm. The freemartin gonads were about two-thirds the length of normal gonads in 7- to 7.5-cm-long fetuses. There was a progressive increase in the length of normal gonads with increasing fetal length, while the length of freemartin gonads did not increase significantly. There was no differentiation of cortex and medulla in freemartin gonads. In the majority of freemartin gonads, the epithelial cell cords resembled medullary cords of the female, but in a few cases some of the cords resembled seminiferous tubules. The tunica albuginea of the freemartin gonad was a compact structure like the tunica albuginea in the normal male. The rete continued to grow in the male and to a lesser extent in the freemartin, while the rete gradually diminished in the normal ovary.

Jost *et al.* (1972) studied 48 presumptive freemartins (obtained 39 to 62 days after breeding) from cows with induced multiple pregnancies. Females were classified as presumptive freemartins when anastomosis of the chorioallantoic circulation had occurred in cases of heterosexual pregnancy. The period of 39 to 62 days was selected because it covers the period of sexual differentiation of the testes to the establish-

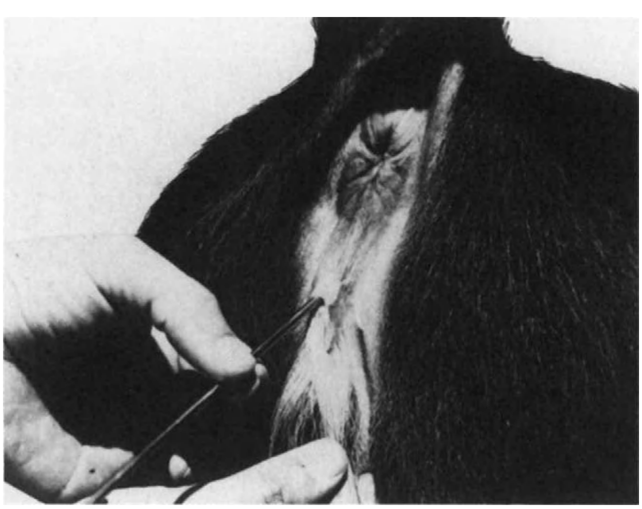

Fig. 2.6. Freemartin heifer with small ventrally displaced vulva and long tuft of vulvar hair. Acc. No. 13312. (Photo from Dr. Francisco Megale, Belo Horizonte, Brazil.)

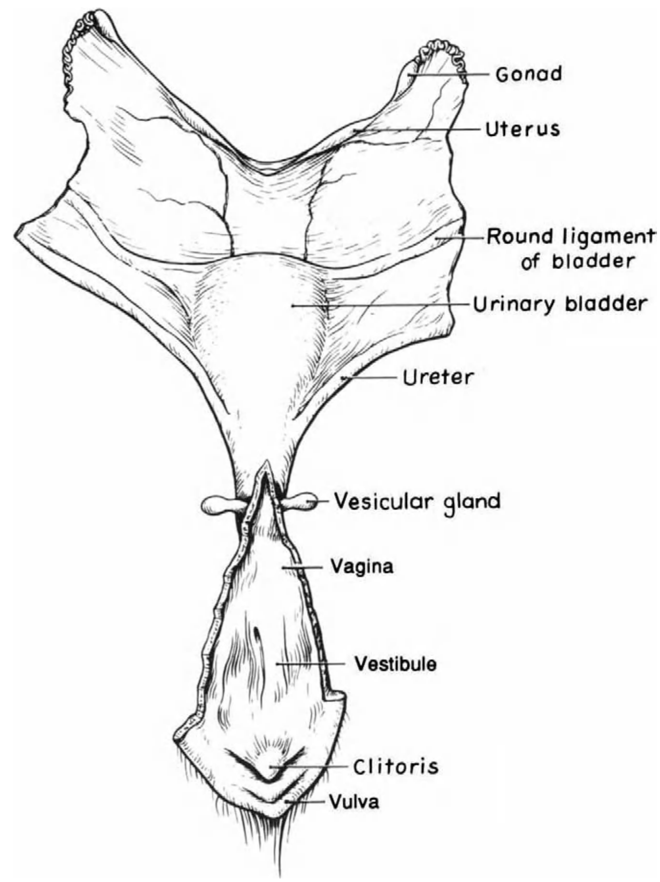

Fig. 2.7. Reproductive organs of bovine freemartin. Acc. No. 1911.

ment of most of the male structures. The gonads of control females and freemartins did not differ in appearance up to 48 days, after which the growth of freemartin gonads practically stopped. Grossly visible alterations were not very obvious before Day 60. The first histologic evidence of freemartinism was observed between 49 and 52 days in all the presumptive freemartins. No seminiferous tubules were present in the gonads of the freemartins. Jost *et al.* suggested that if seminiferous tubules are present, they develop at a later stage. The first gonadal alterations in freemartins appeared several days after the testes were recognizable in male fetuses. Some development of vesicular glands was observed in only three of the freemartins and no prostatic buds were observed in any of the freemartins. Vesicular glands appeared in males on Day 56.

Ohno (1969) recorded the histologic lesions of four pairs of fetal freemartin gonads between the 100th and 125th days of gestation. At this stage of development, the normal fetal ovary consists of three layers: a central gonadal blastema, an intermediate region containing follicular cell cords, and a cortical region with ovigerous cords filled with germ cells (Gropp and Ohno, 1966). Ohno (1969) reported that "initial changes in the differentiation of freemartin gonads take place in the central and cortical regions of the ovary; the intermediate region remains intact." The central region enlarges and the rete ovarii begins to resemble rete testis. The cortical region degenerates and most of the germ cells are destroyed. Connective tissue replaces the cortical region and forms a tunica albuginea. In a highly virilized gonad, gonadal cords (follicular cell cords) become convoluted tubules that resemble seminiferous tubules.

Vigier *et al.* (1977) conducted a histologic study of 82 fetal freemartins at ages of 39 to 250 days postinsemination. They reported that the freemartin condition occurs in two distinct phases. The initial phase is characterized by inhibition of gonadal development and regression of paramesonephric derivatives. This phase begins approximately on Day 50 and is followed by a masculinization phase that may begin on Day 75, but is often later.

The gonads of postnatal freemartins are usually small and the reproductive organs should be removed carefully to avoid leaving one or both gonads in the carcass. The gross appearance of the gonads varies from that of a small testis to an approximately normal-appearing ovary weighing as much as 18 g. In highly masculinized freemartins, the gonads sometimes pass through the inguinal canal and are located in the subcutaneous tissue in the flank (Willier, 1921; Buyse, 1936; Short *et al.*, 1969). A scrotum does not develop. The gonads in highly masculinized cases consist of well-defined seminiferous tubules lined by sustentacular cells and surrounded by interstitial cells (Fig. 2.8). No germinal cells are present in the seminiferous tubules of postnatal animals, although they have been found in the fetal gonad (Vigier *et al.*, 1977).

Willier (1921) described the morphology of the gonads of nine freemartins ranging in age from 5 days to 3 years. The gonads were classified into three groups characterized as low, medium, and high degrees of transformation in the male direction. He considered that the "three groups constitute a chain of connecting links between an embryonic ovary and a testis." The sex cords exhibited a series of gradations between medullary cords and seminiferous tubules. The interstitial cells increased in number as the gonad transformed in the male direction. The degree of penetration of the rete into the gonad also increased with the degree of male transformation. In the most highly transformed gonads, the rete penetrated to the caudal end of the sex-cord region. The gonads in freemartins, in the low and medium groups, were located in the position of normal ovaries. The majority of gonads in the high-transformation group were descended to a position in the subcutaneous tissue of the groin without the development of a scrotum. The highly transformed gonads were larger than the less transformed gonads, but smaller than the testes of normal animals of the same age. The gonads of a 14-month-old highly transformed freemartin measured 40 x 12 mm each. Willier stated that "the most highly transformed sexual cords are typical seminiferous tubules in every respect except that the transformation in the male direction has not proceeded to the production of any stage of male sex cells."

The epididymis was absent in animals exhibiting a low degree of transformation of the gonads. Only the

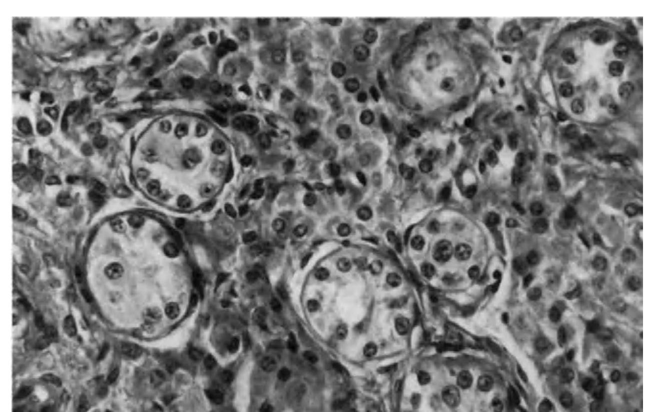

Fig. 2.8. Freemartin gonad. Seminiferous tubules lined by sustentacular cells and surrounded by interstitial cells. ×222. Acc. No. 6942.

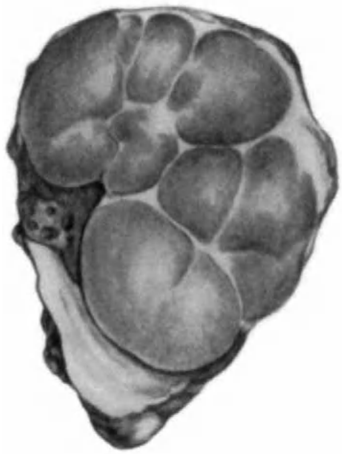

Fig. 2.9. Irregular-shaped masses of interstitial cells in freemartin gonad. Acc. No. 6942.

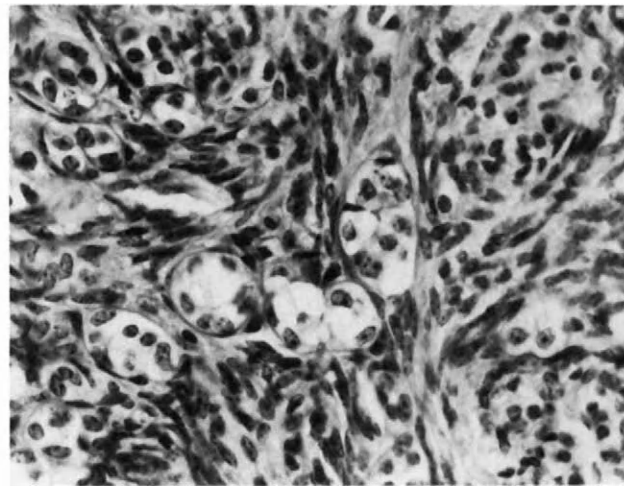

Fig. 2.11. Sex cords and interstitial cells in freemartin gonad. ×326. Acc. No. 2030.

head of the epididymis was present in the intermediate group and a typical epididymis was present in the freemartins with the most highly transformed gonads.

Some freemartins develop large gonads containing follicles and masses of tissue resembling corpora lutea (Fig. 2.9). Oöcytes have been found in some of the follicles (Willier, 1921; Rajakoski and Hafez, 1963). The luteal or interstitial cell masses (Fig. 2.10) vary in size from approximately 1 mm to those as large as normal corpora lutea and are usually multiple. Luteinization of atretic follicles occurs in some freemartins. Settergren (1964) found during a study of ovarian morphology in cases of bovine gonadal hypoplasia that "when the number of follicles in a pair of ovaries was very low . . . there were disturbances in the follicular development in the form of luteinization without ovulation and the formation of interstitial gland-like masses." This principle may apply to freemartins that have only a few follicles and develop masses of luteal or interstitial gland tissue.

Sex cords (Fig. 2.11) are distributed throughout the gonads of freemartins. The cords may become cystic (Fig. 2.12) or hyperplastic (Figs. 2.13 and 2.14). Herzog (1967) reported the presence of intratubular concrements in the gonads of freemartins. Similar bodies are present in the testes of some cryptorchid animals, especially horses.

The rete is usually prominent in an eccentric position. In small gonads it may constitute a large portion of the organ. Absence of gonads has been reported by Swett *et al.* (1940) and Laster *et al.* (1971). At least some of the reported cases may be questionable. As mentioned earlier, the reproductive tract of the free-

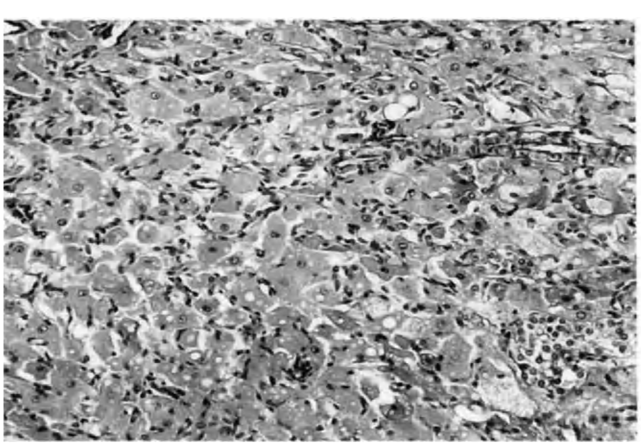

Fig. 2.10. Interstitial cells in freemartin gonad. ×89. Acc. No. 14964.

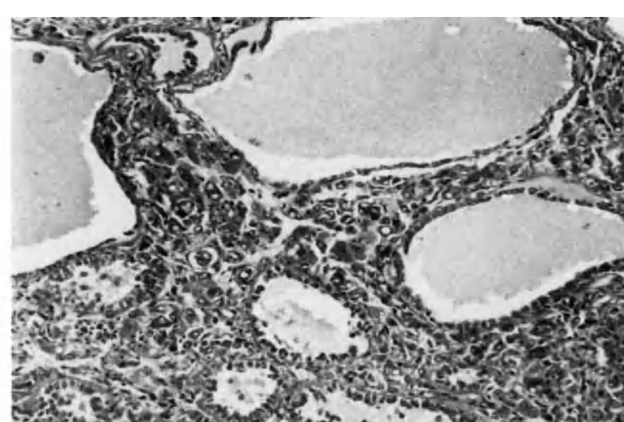

Fig. 2.12. Cystic sex cords in freemartin gonad. ×89. Acc. No. 6942.

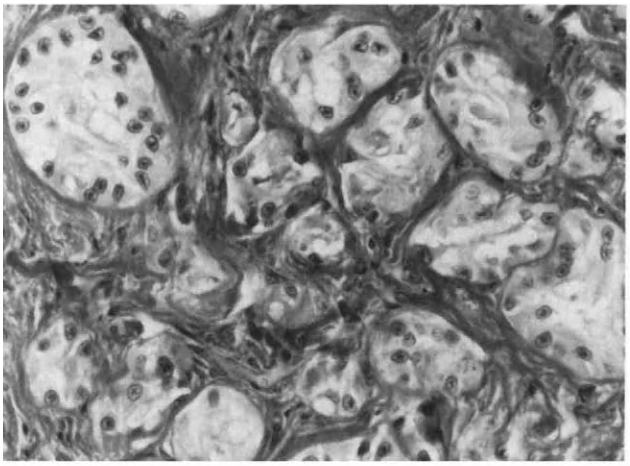

Fig. 2.13. Hyperplastic sex cords in freemartin gonad. ×204. Acc. No. 14960.

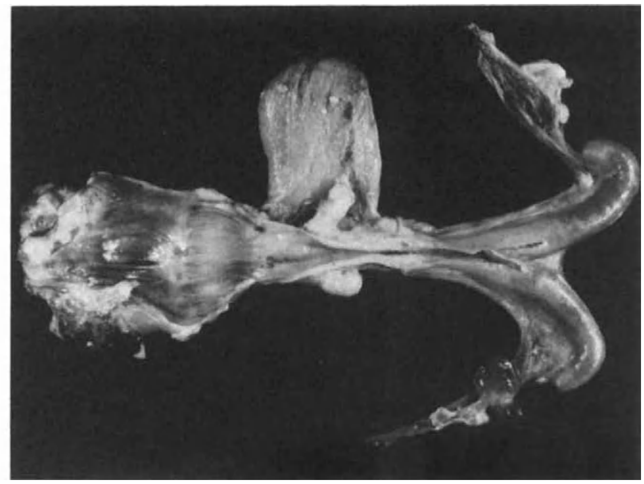

Fig. 2.15. Freemartin uterus that communicates with the vagina. Acc. No. 19236.

martin must be removed with care and a thorough search made for gonadal tissue. The gonads may be very small, located some distance from the rest of the reproductive organs and even descended into and through the inguinal canal. Careful histologic examination of any nodules of tissue associated with the cranial part of the reproductive tract may be necessary to determine whether gonadal tissue is present.

The degree of regression of the paramesonephric derivatives varies considerably. In highly masculinized individuals, the paramesonephric duct derivatives may be completely lacking cranial to the vestibule of the vagina. At the other extreme, a well-developed, but somewhat small, uterus may be present that communicates with the vagina (Fig. 2.15). The cervix usually does not develop. The vagina is of normal size caudally but rapidly tapers cranially. Uterine tubes have been reported by Rothe *et al.* (1961) and Laster *et al.* (1971), but are rare in freemartins.

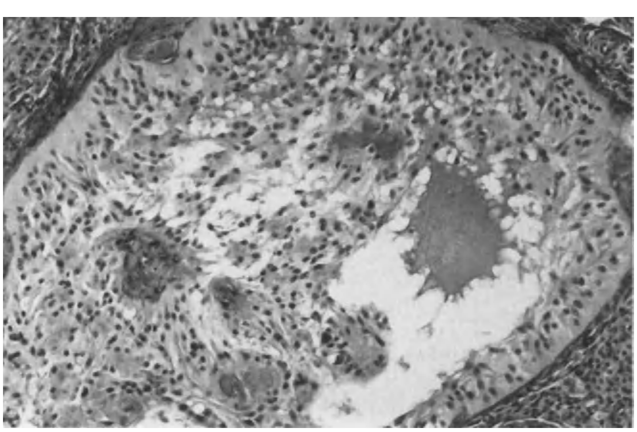

Fig. 2.14. Hyperplastic sex cord in freemartin gonad. ×89. Acc. No. 14964.

Vesicular glands are present in the majority of freemartins and are useful in differentiating freemartinism from severe cases of aplasia of the paramesonephric duct derivatives. Two pairs of vesicular glands are occasionally present (Fig. 2.16) but freemartins rarely have prostatic tissue. The vesicular glands consist of relatively few alveoli lined by low cuboidal epithelium in a prominent fibrous tissue stroma (Fig. 2.17).

Smith *et al.* (1977) reported a fertile female born co-twin to a male calf. Since both XX and XY cells were in the blood of the heifer, they concluded that anastomosis of the chorioallantoic circulation had occurred. They suggested that the fertility of this heifer may have been due "to the establishment of vascular anastomoses in the fetal membranes after the critical period in gonadal differentiation in the female fetus."

Wijeratne *et al.* (1976) presented evidence for the occurrence of sterility associated with single-birth freemartinism in heifers. They determined the karyotypes from peripheral blood cultures on 36 heifers that did not conceive to at least three inseminations. Twelve of the heifers were found to have chimerism. Five of the 12 were singletons. The clinical histories and postmortem findings in the five singleton chimerics were presented; three had reproductive organs characteristic of freemartins, and the other two had well-developed ovaries and tubular organs. One had bilateral segmental aplasia of the uterus and the other had an imperforate cervix.

Dunn *et al.* (1979) conducted cytogenetic and reproductive studies on 22 bulls born co-twin with freemartins. Semen was evaluated and breeding records were studied on 12 bulls from one artificial insemina-

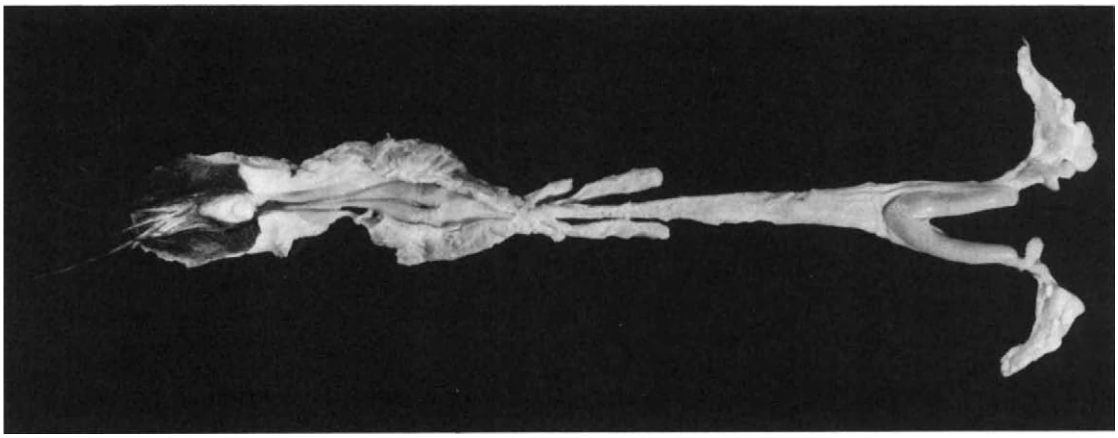

Fig. 2.16. Freemartin reproductive tract with two pairs of vesicular glands. Acc. No. 17689.

tion (A.I.) center. "Seven (58.3%) of the 12 A.I. chimeric bulls were reproductive culls as compared to only 5.4% of their 128 controls ($P < 0.001$). The culled chimeras either produced no semen, had a low sperm count or had a high incidence of abnormal spermatozoa." The seven bulls with fertility problems had more numerous focal areas of testicular degeneration than the controls. The presence of lymphocytic foci in the interstitial tissue of the testes of the chimeric bulls suggested an autoimmune response. The XX lymphocytes in the peripheral blood of the 22 chimeric bulls ranged from 5 to 95% of the total lymphocyte population. No relationship was found between the percentage of XX blood cells and the reproductive capacity of the bulls. In their review of the literature, Dunn *et al.* (1979) provided references to other chimeric bulls with reproductive problems and references to chimeric bulls with normal fertility.

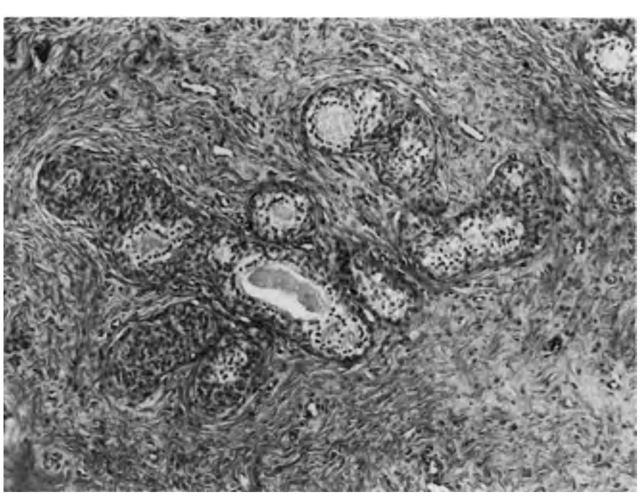

Fig. 2.17. Vesicular gland of a freemartin. ×81. Acc. No. 6942.

Marcum (1974) summarized data on XX/XY chimerism in 124 female and 93 male calves from 129 heterosexual twin births. The report included data published by others as well as his own. He found "a very highly significant positive correlation between the percentage of XY cells in chimaeric females and the percentage of XY cells in males from the same cosibship ($r = 0.97$; $P < 0.001$)." Marcum *et al.* (1972) examined the reproductive tracts of 17 freemartins and found no definite relationship between the degree of masculinization of the reproductive organs and the percentage of male chromosomes in the peripheral blood.

Greene *et al.* (1977) determined the karyotypes of 18 freemartins at 1, 24, and 52 weeks of age and found that they averaged 60.7, 57.9, and 55.5% XY cells, respectively. No relationship was found between the proportion of XY cells and the degree of masculinization. They concluded that there is "convincing evidence that the blood lymphocyte XX : XY karyotype ratio (1) is not related to the degree of masculinization and (2) is stable in the postnatal freemartin."

Although the absence of XY cells appears to be rare in freemartins, Dunn *et al.* (1981b) found no XY cells in 300 metaphases from each of 2 (2.9%) of 70 freemartins. They estimated that the "mean and standard deviation of XY cell frequency in 70 freemartins (12,885 metaphases) was 0.48 and 0.30, respectively. These values indicate that sample sizes of 28 and 168 are required to be 95% and 99% confident, respectively, that a female co-twin will not be misclassified."

Freemartin Sheep

Bruère and Macnab (1968) recorded six cases of freemartinism in sheep. Chromosome studies revealed that these sheep had blood cells chimerism. They stated that "freemartinism is probably more common in sheep than has been suspected previously." All the sheep had female external genitalia with enlargement of the clitoris. They reported that the gonads were similar to those of the bovine freemartin. Partial uterine development was present in two of the six. Dain (1971) conducted a survey of sex chimerism in the lymphocytes among 161 sets of heterosexual pregnancies in sheep. The sex of the karyotype was used as the criterion for diagnosing freemartinism. Two (1.2%) chimeric sets were found. This is in agreement with Bruère and Macnab's (1968) suggestion that freemartinism may be more common in sheep than has been suspected.

Freemartin Goats

Ilbery and Williams (1967) presented evidence for the existence of freemartinism in the goat. Their case was a genetically polled, Saanen, chimeric intersex born co-twin with a male. The gonads were located in the inguinal region and resembled hypoplastic testes, being about one-third normal size. It had a vulva, large clitoris, epididymides, and vesicular glands, but no development of paramesonephric derivatives.

Bon Durant *et al.* (1980) reported a probable case of freemartinism in an American La Mancha doe that was examined because of anestrus. The goat was a triplet to two male offspring. A vaginal speculum could not be inserted more than 2 cm cranial to the vulva. Neither tubular nor gonadal parts of the reproductive system could be seen on exploratory laparotomy. Examination of an aspirate of bone marrow revealed the presence of hematopoietic chimerism.

Freemartin Swine

Bruère *et al.* (1968) described 1 intersex pig in a litter of 13 consisting of 8 males and 4 females in addition to the intersex. The gonads had descended but no scrotum was present. The vulva was slightly enlarged at the ventral commissure. The gonads were small and on histologic examination resembled cryptorchid testes. The epididymides were relatively large and vesicular glands were present, but the paramesonephric derivatives had not developed. They thought that the evidence was suggestive, but not conclusive, that the animal was a freemartin.

Testicular Feminization

Testicular feminization is an inherited form of male pseudohermaphroditism that is transmitted by females to half their male offspring. The phenotypically female individuals have vulvar development, retained testes, and failure of development of the mesonephric and paramesonephric derivatives. Male accessory reproductive organs do not develop because of end organ insensitivity to androgens (Bardin *et al.*, 1973; Bardin and Bullock, 1974). Testicular feminization has been described in man (Morris, 1953), rats (Stanley and Gumbreck, 1964; Stanley *et al.*, 1973), mice (Lyon and Hawkes, 1970; Ohno and Lyon, 1970), the dog (Schultz, 1962), cat (Meyers-Wallen *et al.*, 1989), cattle (Nes, 1966), swine (Lojda, 1975; Wensing *et al.*, 1975), sheep (Bruère *et al.*, 1969b), and in a Quarter Horse (Kieffer *et al.*, 1976).

Short (1969) reviewed John Hunter's report "Account of the Freemartin," which was published in 1779. According to Short, "Mr. Wright's freemartin," described by Hunter, had the anatomical features of an animal with testicular feminization. It had large retained testes, rudimentary male and female internal reproductive organs, a fairly well-developed udder, and a vulva. Therefore it appears that the first case of testicular feminization was described in cattle approximately 200 years ago by one of the founders of the Royal Veterinary College in London.

Nes (1966) reported three cases of testicular feminization among eight offspring of a Norwegian Red cow. According to Nes, "the hermaphrodites had well-developed udders, female external genitalia, rudimentary female and male genital ducts and intra-abdominal testes." Rieck (1971) described a case of testicular feminization in a Friesian heifer and Long (1981) reported a case in an Ayrshire cow.

I have examined one case of apparent testicular feminization in a single-born, 4-year-old, Guernsey male pseudohermaphrodite. It had a well-developed vulva and vestibule but no other accessory reproductive organs. The testes were located in the abdominal cavity and weighed 54 g each (Fig. 2.18). The testes were composed of seminiferous tubules, lined by stratified sustentacular cells, and numerous well-differentiated interstitial cells (Fig. 2.19). Focal areas of interstitial cell proliferation occurred in both gonads and could be interpreted as hyperplasia or early neoplasia.

Drug-Induced Intersexuality

The administration of androgens and many progestins to pregnant females induces masculinization of the genitalia in female offspring of rats, mice, guinea pigs, rabbits, cattle, sheep, dogs, monkeys, and women. Some masculinization of the external genitalia of the female rat fetus results from treatment with estrogens during late pregnancy. Feminization of the reproductive tract and external genitalia of the male rat fetus can be induced with estrogens, some progestins, and antiandrogens (Saunders, 1968).

Jost *et al.* (1963) injected testoterone proprionate or 17-methyl testosterone intramuscularly into preg-

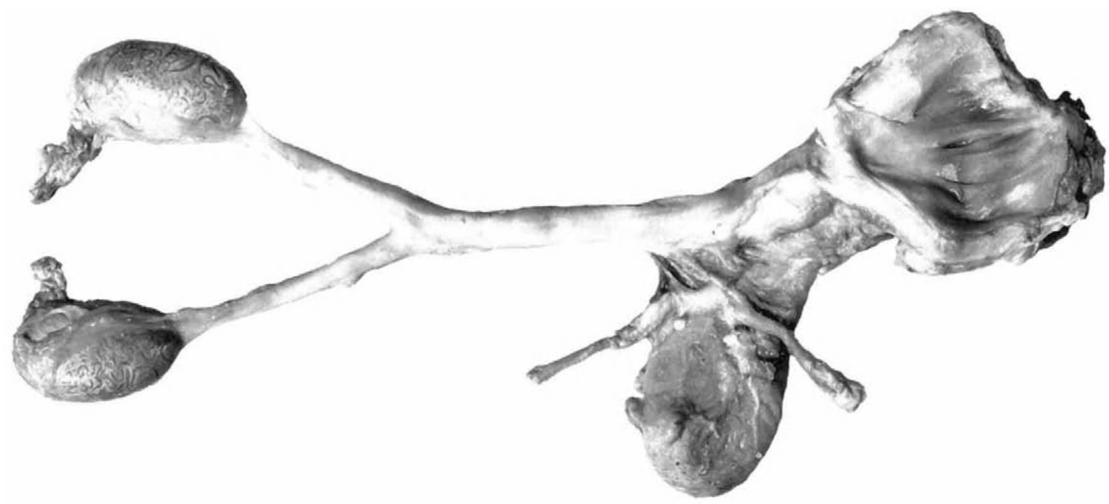

Fig. 2.18. Reproductive tract from a bull with testicular feminization. Acc. No. 2190.

nant cows from 35 to 42 days after breeding and continuing until 105 to 110 days when the cows were destroyed. The external genitalia of the female fetuses were masculinized but the internal reproductive organs consisted of normal female structures.

The feeding of methyl testosterone (150 μg/kg body weight/day) to female dogs, beginning on the first day of mating and continuing throughout pregnancy, induced intersexuality in all 42 female offspring from 14 bitches (Shane *et al.,* 1969). The male offspring were normal. The female pseudohermaphrodites had an increase anogenital distance, a "small penis-like protuberance," which in some cases was hypospadiac. A normal vulva was absent and urine was voided through an underdeveloped penis. There was no scrotal development. The genital tract was normal proximal to the vestibule of the vagina. The ovaries became functional, with the development of corpora lutea, in the female pseudohermaphrodites that were kept until maturity. The uterine tubes, uterus, and cranial vagina were normal.

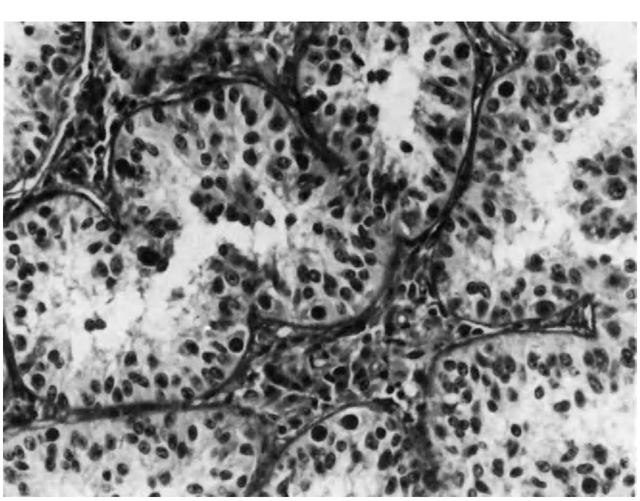

Fig. 2.19. Stratification of sustentacular cells in gonad of a bull with testicular feminization. ×204. Acc. No. 2190.

The injection of testosterone enanthate into pregnant ewes, beginning 25 to 45 days postbreeding, modified the reproductive tracts of the female offspring (Alifakiotis *et al.,* 1976). The ovaries, uterine tubes, uterus, and cranial vagina were normal. Masculinization included development of epididymides, vesicular glands, prostate, bulbourethral glands, scrotum, and penis.

Wilson and Tarttelin (1978) gave ewes "intramuscular injections of testosterone cypionate (200 mg) on each of the 20th, 27th and 40th days of gestation." The male lambs were anatomically normal at birth. The female offspring "displayed complete external genital masculinization including the presence of a prepuce, penis and scrotum and the absence of an external vulval opening." Epididymides, vesicular glands, and other male secondary sex glands were not found. The ovaries, uterine tubes, uterus, cervix, and vagina appeared to be normal.

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Chapter 3
The Ovary

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Bibliography

Anatomic Features

"The Viscera of Domestic Mammals" by Schummer, Nickel, and Sack (1979) is recommended for the gross anatomy of the ovaries of domestic mammals.

The poles of the ovary are known as the tubal and uterine extremities. The ovary is composed of an outer layer, the cortex (zona parenchymatosa), and an inner core, the medulla (zone vasculosa). The cortex contains follicles, corpora lutea, and stromal tissue with its blood vessels and lymphatics. A dense layer of fibrous tissue, the tunica albuginea ovarii, is located between the outer cortex and the surface epithelium. Although the term "germinal epithelium" is commonly used for the surface epithelium, it is a misnomer because the covering epithelium is modified peritoneum and does not give rise to germinal cells.

The medulla consists of large, tortuous blood vessels, lymph vessels, nerves, and supporting connective tissue. A sharp border does not exist between the cortex and medulla. The rete ovarii, which is the homologue of the rete testis, is located in the hilar portion of the tubal extremity of the ovary and extends into the mesovarium. Medullary cords and tubules are scattered in the connective tissue around the rete. Remnants of mesonephric tubules are present in the mesovarium adjacent to the rete ovarii. Abundant smooth muscle is present in the mesovarium and occasionally gives rise to leiomyomas.

Follicles are classified according to their stage of development: primordial, primary, secondary, and vesicular. A primordial follicle consists of an oöcyte surrounded by stromal tissue or a single layer of squamous cells. A primary follicle is one in which the layer of squamous cells has transformed into a single layer of low columnar granulosa cells. A secondary (growing) follicle has multiple layers of granulosa cells but no antrum. A vesicular (Graafian or tertiary) follicle has an antrum. During follicular atresia the granulosa cells undergo pyknosis and karyorrhexis. The nuclear fragments and pyknotic nuclei float into the follicular fluid. This necrotic debris has been misinterpreted, by some, as an inflammatory exudate. During follicular maturation the theca becomes prominent. The inner layer of theca cells (theca interna) hypertrophies and the more peripheral theca cells (theca externa) remain fibrous in appearance.

Polyovular Follicles and Polynuclear Oöcytes

Polyovular follicles (follicles with more than one oöcyte, Fig. 3.1) and polynuclear oöcytes occur in all species of domestic mammals but are more common in the dog and cat than in the other species (Hartman, 1926; Shehata, 1974b). They are more common in young than in aged animals. Hadek (1958) found polyovular follicles in ovaries of sheep to be limited

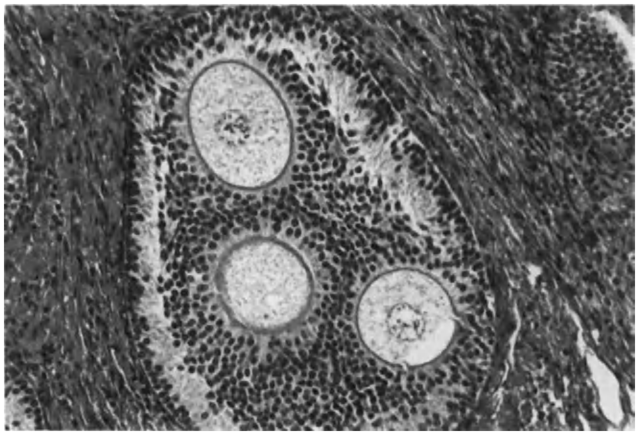

Fig. 3.1. Polyovular follicle in the ovary of a 7-month-old bitch ×178. Acc. No. 18279.

to animals slaughtered during proestrus, estrus, and metestrus and not those in diestrus.

Interstitial Glands

Interstitial gland cells occur in the ovaries of all species of domestic animals but many details concerning them are still unknown. Mossman and Duke (1973a) consider interstitial cells to be "any endocrine-type glandular cells occurring in the ovary or mesovarium other than those of the theca interna of normal ripening follicles (thecal gland) and the corpus luteum (luteal and paraluteal glands). They have been tentatively divided into seven types, based on their morphology, location, cellular origin, fate, and correlation of their state of glandular differentiation with the age and reproductive condition of the female. The seven types are fetal, thecal, stromal, medullary cord, rete, gonadal adrenal and adneural. . . . Intergradation between some of these types is no doubt a fact."

The fetal type is especially prominent in equine fetal gonads. The thecal type occurs in all species of mammals but is not very conspicuous in most artiodactyles. It differs from the thecal gland cell of the normal ripening follicle in that it differentiates from the theca interna of atretic follicles. The cells become very prominent in women during the last month of pregnancy. "Since follicles still develop and degenerate after the reproductive age, thecal-type interstitial tissue still occurs; this is particularly obvious in the ovaries of women." Gonadal adrenal tissue is very common in and around equine gonads and occurs occasionally in other species of domestic mammals. The rete and medullary cord types of interstitial gland tissue occur in the ovaries of domestic mammals that have severe ovarian hypoplasia. "The medullary cord type is particularly well differentiated in the mink and some other mustelids. . . . Stromal-type interstitial gland tissue is unusually abundant in several groups, notably rabbits and hyraxes" (Mossman and Duke, 1973a).

Bovine Ovary

The ovary of the cow is oval and weighs between 3 and 18 g. Salisbury and Van Demark (1961) gave the following average measurements for the ovaries of European breeds of cattle: 3–42 mm long, 19–32 mm broad, and 13–19 mm thick. Lamorde and Kumar (1978) reported that the average size of the ovary of the zebu *(Bos indicus)* cow is 23 x 18 mm, which is smaller than that of European *(Bos taurus)* cattle. Rajakoski (1958) examined 1500 pairs of ovaries from Swedish Red and White cattle and reported that the average ovarian weight varied at different times of the year for the right ovary between 10.2 and 11.4 g and for the left ovary between 8.3 and 9.4 g. Eriksson (1943) reported that in normal Swedish Highland cattle, over 1 year old, the right ovary weighed 7.66 ± 0.41 g and the left ovary weighed 7.08 ± 0.41 g. The size varies according to the stage of the estrous cycle, stage of pregnancy, age, and general condition of the animal. The right ovary is usually slightly larger than the left because of the greater physiologic activity of the right ovary, which ovulates in approximately 60% of estrous cycles.

From a detailed study of the morphology of the ovarian follicular system, Rajakoski (1960) concluded that oögenesis in cattle is completed by birth. Atresia of primary follicles, which is observed only occasionally, is recognized by chromatolysis of the nucleus and shrinkage and phagocytosis of the oöcyte. Atresia of secondary follicles is characterized by hyalinization of the more highly developed zona pellucida. In vesicular follicles atresia begins with degeneration of the granulosa cells. A hyalin layer develops between the remnants of the degenerating granulosa and the degenerating theca. The antrum becomes completely obliterated, resulting in the formation of a corpus atreticum. In large vesicular follicles a cyst remains and is not obliterated until after complete degeneration of the follicular wall. The granulosa cells do not have a direct blood supply but the theca interna is well supplied with blood vessels. Rajakoski (1960) reported that two waves of follicular growth occur during the estrous cycle, the first occurring during the third and fourth day of the cycle (estrus referred to as Day 1). The largest follicle (7–12 mm) from the first growth phase undergoes cystic atresia after the eleventh day of the cycle. The second wave begins on the twelfth day of the cycle when the follicles from the first wave begin to undergo atresia. The mature bovine follicle is approximately 16 to 19 mm in diameter.

A small amount of hemorrhage occurs following ovulation. The weight and progesterone content of the corpus luteum "increase rapidly between Days 3 and 12 of the cycle and remain relatively constant until Days 16 to 18 of the cycle, after which rapid regression occurs" (Hansel and McEntee, 1977). The delta (gonadotrophic) cells of the adenohypophysis become heavily granulated during regression of the corpus luteum (Jubb and McEntee, 1955).Rapid and nearly complete degranulation of the delta cells occurs shortly after the onset of standing estrus. Degranulation of the delta cells does not occur in cows that fail to ovulate.

The corpus luteum of pregnancy is larger than the cyclic corpus luteum. Edwards (1962) reported that cyclic corpora lutea of cattle had a mean diameter of 23 mm and a mean weight of 5.71 g, whereas corpora lutea of pregnancy had a mean diameter of 24.6 mm and a mean weight of 6.52 g. The corpus luteum of pregnancy reached its maximum size (7.21 g mean weight) at approximately two to three months of gestation, then regressed until about four to six months and remained about this size (6.14 g mean weight) until term.

The corpus luteum rarely, if ever, persists in cattle unless pregnancy ensues or some pathologic uterine condition is present. Diseases associated with persistence of the corpus luteum include mummification of the fetus, pyometra, hydrometra (secondary to malformations of the cervix), and failure of endometrial gland development.

The corpus luteum of pregnancy does not persist in cattle following parturition. It begins to degenerate before the onset of parturition and within a few days after parturition the corpus luteum is in an advanced stage of degeneration. Most normal dairy heifers and cows ovulate at least once by 30 days postpartum. The first development of a large follicle, and subsequent ovulation, occurs approximately 15 to 17 days postpartum in many dairy cows. The next cycle may be slightly shortened, varying from 10 to 18 days with an average of about 17 days. Webb *et al.* (1980) reported that "During the first oestrous cycle after parturition there was a significantly shorter period when plasma progesterone levels were elevated than during the next two cycles." Folman *et al.* (1973) studied the relationship between plasma progesterone concentration and conception in postpartum dairy cows. They found that cows that conceived to one service had significantly higher progesterone levels during the estrous cycle preceding insemination than cows that did not conceive.

Ovine Ovary

The ovary of the ewe is approximately 10 to 15 mm long and almond-shaped. The mature follicle is 8 to 10 mm in diameter. The corpus luteum is reddish pink during the early part of the cycle but becomes pale as the next estrus approaches.

Brand (1970) studied the histologic and biochemical changes in the ovaries of sheep during the estrous cycle. The weight of corpora lutea increased slowly until Day 3 and then rapidly until Day 10. It remained constant until Day 14 and then decreased rapidly.

O'Shea *et al.* (1977) reported changes in the small blood vessels of the corpus luteum of the ewe during regression of luteal tissue. Degenerative vascular lesions were observed first on Day 14 and were consistently present on Day 16 of the cycle. Degenerative changes occurred in the capillaries, and cellular debris was found in many capillaries and venules.

Small and large luteal cells occur in the corpora lutea of sheep, cattle, and swine. Histologic evidence suggests that the large luteal cells develop from granulosa cells and the small luteal cells from the theca interna (Donaldson and Hansel, 1965; O'Shea *et al.*, 1980). Fitz *et al.* (1982) investigated the steroidogenic activity of large and small luteal cells in the corpus luteum of the ewe. They reported that "The large luteal cells appear to secrete most of the progesterone produced by the corpus luteum; however, this secretion appears to be independent of LH and dbcAMP (O^2-dibutyryladenosine 3′ : 5′-cyclic monophosphoric acid). In contrast, the small luteal cells secrete minimal quantities of progesterone in the unstimulated state but respond dramatically to LH or dbcAMP."

Porcine Ovary

The sow has a mulberry-shaped ovary that weighs 7 to 20 g and is 30 to 60 mm long. Follicles and corpora lutea bulge from its surface. Mature follicles in the sow are 8 to 10 mm in diameter. The follicular cavity becomes filled with blood and serum following ovulation. The accumulation of fluid distends the cavity of ovulated follicles so that they may be larger than prior to ovulation. The corpus luteum of the sow does not contain pigment. Its maximum size is approximately 12 mm. The regressing corpus luteum has a more collagenous appearance than regressing corpora lutea of other species of domestic mammals. Akins and Morrissette (1968) and Schnurrbusch *et al.* (1975) described and illustrated the gross ovarian changes during the estrous cycle of swine.

Unsicker (1971) described the ultrastructure of the medullary cords in the ovary of immature and mature sows. The ovary of immature animals had both cords and tubes, some of which contained colloid. Mature sows had only medullary tubes lined by cuboidal or columnar, sometimes pseudostratified, epithelium. Unsicker stated that "Because of morphological similarities between granulosa cells and main cells of the medullary cords it is assumed that both have a similar function" (referring to steroid function).

Equine Ovary

The ovary of the mare is kidney bean-shaped with a notchlike depression, the ovulation fossa (ovarian fossa), on the ventral or free border. Ginther (1979) reported that the mean, combined, ovarian weight of 50 horse mares was 123 g and that of 38 pony mares was 43.8 g. The mean dimensions of 133 horse mare ovaries were 51.6 mm long, 28.5 mm wide, and 32.7 mm high.

The ovary of the mare has many unusual features in comparison to the ovaries of other domestic mammals. The relatively small ovulation fossa is the only area through which ovulation can occur (Witherspoon and Talbot, 1970; Witherspoon, 1975). The mesovarium extends for a considerable distance over the surface of the ovary. The zona parenchymatosa (cortex), which contains the follicles, is a gray, caplike, thin layer of tissue on the surface of the fetal gonad. As the animal matures, the zona parenchymatosa extends into the center of the gonad, displacing the zona vasculosa (medulla) to the periphery. The ovarian stroma has a very fibroblastic appearance and large areas may be devoid of follicles. The abundant interwoven bundles of stromal tissue in the equine ovary are sometimes mistaken for a neoplasm. The mature follicles may be as large as 70 mm (Aiken, 1926) and should not be diagnosed as cystic, since follicular cysts that are similar to those in the cow and sow do not occur in the mare. Ginther (1979) mentioned that the range of maximum diameter of preovulatory follicles is great and may vary from approximately 20 to 60 mm. Hughes *et al.* (1980) reported that "The follicle destined to ovulate usually begins to increase in size prior to the onset of estrus and averages about 45 mm in diameter the day before ovulation. Occasionally, an anovulatory follicle will develop to a size of ten cm or more, persist for a variable time over a period of several cycles, and then regress. These persistent follicles do not interfere with the occurrence of normal estrous cycles, including ovulation." Arthur (1958) reported a 10-cm follicle in a pregnant mare. Ginther presented presumptive evidence for a two-wave theory of follicular growth during diestrus in the mare. The theca cells undergo degeneration prior to ovulation and do not contribute to the formation of the corpus luteum.

A large corpus hemorrhagicum, 70% the size of the preovulatory follicle, forms following ovulation. A small amount of luteal tissue bulges above the ovulation fossa for only a few days and then sinks into the ovary. During pregnancy, secondary corpora lutea begin to form at about Day 40. The number of secondary corpora lutea varies considerably among mares. Squires and Ginther (1975) stated that "the primary CL and secondary CL begin to regress after Days 140 to 160 and are completely atrophic by Day 210 to 220. . . . The long life span of the primary CL demonstrated in our experiments is inconsistent with the generally accepted view that the primary CL regresses early in pregnancy and is replaced by secondary CL." They could detect no difference in the appearance of the primary and secondary corpora lutea. The ovaries of the mare are inactive throughout advanced pregnancy and become smaller than the gonads of the fetus.

Stangroom and Weevers (1962) found a heparin-like anticoagulant in the follicular fluid of the mare. Palla (1952) reported the presence of a similar anticoagulant in the follicular fluid of women, sows, cows, bitches, and rabbits. If such a factor were not present, the ovum could become trapped in a plasma clot following ovulation.

Prominent vessels are present on the surface of the equine ovary. These vessels do not have the support that they would if they were embedded in connective tissue of the medulla as in other species of animals. Therefore, the superficial veins undergo dilatation and form varicosities (Fig. 3.2) in some aged mares.

I am not aware of a description of the rete ovarii in the mare but rete tubules are present in the ovarian tissue near the epoöphoron.

Canine Ovary

The ovary of the bitch is oblong, approximately 15 to 30 mm long, and completely enclosed within the ovarian bursa. Except for a small round area on the

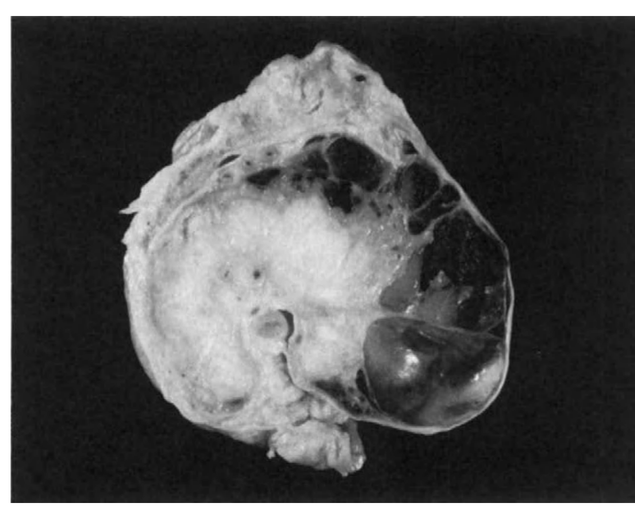

Fig. 3.2. Varicose veins near the surface of an equine ovary. Acc. No. 8665.

lateral surface of the ovarian bursa, the mesosalpinx contains a large amount of adipose tissue and hides the ovary from view. A portion of the ovary can be seen through the small clear area of the mesosalpinx. The opening to the ovarian bursa is a small slit 2 to 15 mm long located on the medial side. The contour of the mature ovary is irregular because of the presence of follicles and corpora lutea, and becomes increasingly so with advancing age. Mature follicles are 5 to 8 mm in diameter (Concannon *et al.*, 1977). Follicles that are destined to ovulate undergo elaborate infolding of the follicular wall during proestrus (Fig. 3.3). In contrast to other domestic mammals, some granulosa cells frequently persist following atresia of large follicles and form granulosa cell cords or islands (Andersen and Simpson, 1973; Stott, 1974). These are oval to elongated masses of cells that somewhat resemble sustentacular (Sertoli) cells of the testis (Fig. 3.4).

A characteristic feature of the canine ovary is the presence of tubular ingrowths of the surface epithelium (Fig. 3.5). Harrison and Matthews (1951) examined ovaries from 106 different species of mammals for the presence of "sub-surface crypts, lined by germinal epithelium which penetrate into, or pass through the tunica albuginea." In domestic mammals ovarian subsurface crypts are present only in the dog. These structures are present in the ovaries of a number of other species of carnivores and in marsupials, seals, elephants, and primates. O'Shea (1966) called the crypts subsurface epithelial structures (SES) and his terminology has been adopted for this book. Estrogen induces hyperplasia of the SES and the SES give rise to cysts and neoplasms.

A prominent rete ovarii is present in the medulla adjacent to the hilus and is surrounded by medullary cords. According to Andersen and Simpson (1973), the rete ovarii of the bitch increases in size during estrus and pregnancy and decreases during metestrus and anestrus. They stated that "Throughout gestation the rete ovarii continues to be enlarged and consists of patent tubules which extend a considerable distance into the mesovarium. The enlarged and dilated tubules have an epithelium of irregular thickness, frequently forming small papillary ingrowths." They also reported that "The rete ovarii in 10% of Beagles over eight years of age contained cysts of variable size; in another 5% the structure was greatly enlarged. Single to multiple cysts in tubules of the rete ovarii can vary from 0.1 to 1 cm or more in size, and upon occasion the cystic condition of the structure distorts the entire ovary. Hyperplasia of a small portion of the rete ovarii is frequently observed in aged Beagles; in some instances the entire rete enlarges and appears as a lobulated tumorous mass in the medulla of the ovary."

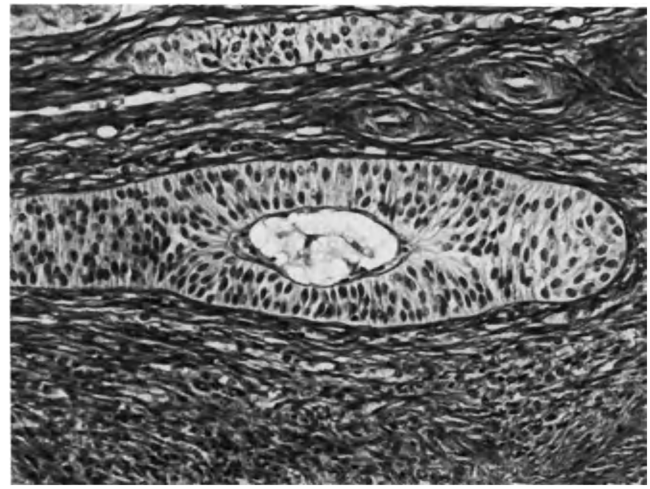

Fig. 3.4. Degenerate zona pellucida in a canine granulosa cell island. ×213. Acc. No. 16473.

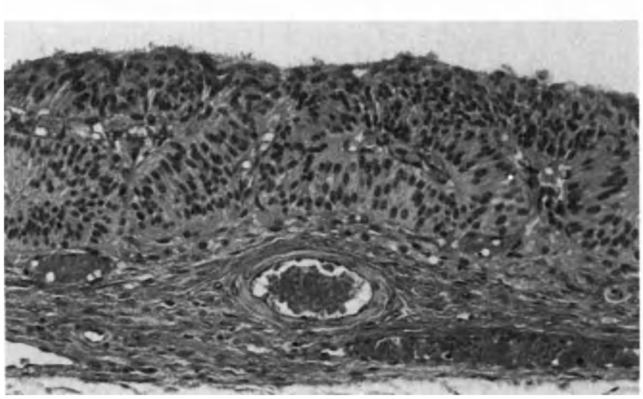

Fig. 3.3. Infolding of granulosa cells in a mature canine follicle. ×178. Acc. No. 8063.

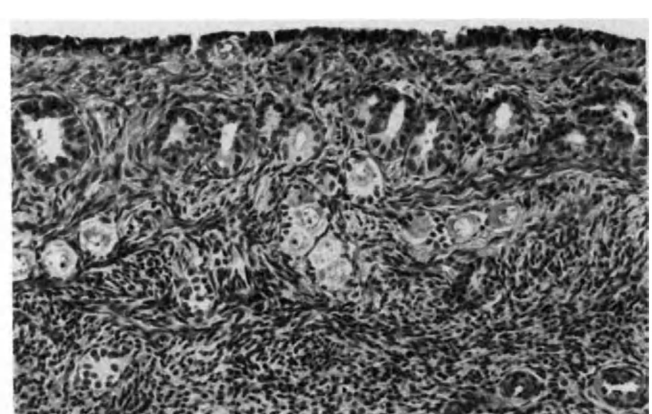

Fig. 3.5. Subsurface epithelial structures in canine ovary. ×178. Acc. No. 16478.

Feline Ovary

The ovary of the queen is oval and 8 to 9 mm long. Mature follicles are 2 to 3 mm in diameter (Foster and Hisaw, 1935). In contrast to the bitch, the mesosalpinx of the queen does not contain adipose tissue and covers only the lateral surface of the ovary. Prominent interstitial gland cells (Fig. 3.6) develop around follicles undergoing atresia (Kingsbury, 1914). The hilus contains a prominent rete ovarii.

Congenital Anomalies

Ovarian Fusion

I have seen one case of ovarian fusion in a term bovine fetus. The gonad consisted of a triangular-shaped mass of ovarian tissue located between the uterine tubes. The apex of the fused ovary was near the proximal ends of the uterine horns (Fig. 3.7). The fetus had multiple other defects, including a single kidney, atresia of the anus, and herniation of the intestines through an enlarged umbilicus.

Anomalies in Position

The position of the ovary varies according to the length of the broad ligament. Cows may have a short, broad ligament on one side resulting in an ovary located closer to the body wall than normal. In cows with uterus unicornus the gonad on the affected side is frequently located near the uterus. On the other hand, in the bitch with uterus unicornus, the ovary is often located some distance from the uterus. In these cases the ovary is occasionally overlooked during ovariohysterectomy.

Fig. 3.7. Fused ovaries in a term bovine fetus with a single enlarged left kidney. Acc. No. 8792.

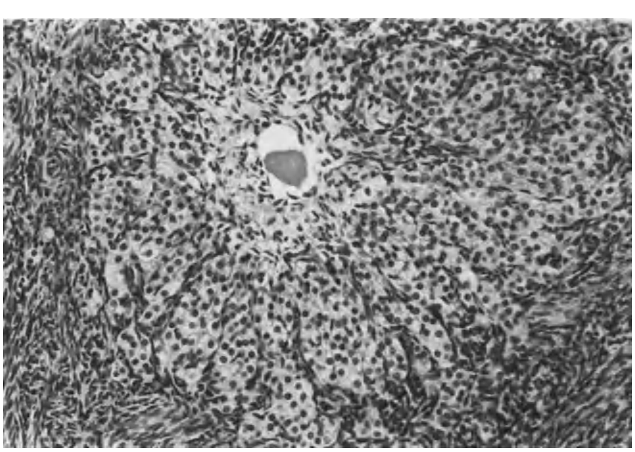

Fig. 3.6. Interstitial gland cells surrounding remains of an atretic follicle in feline ovary. ×178. Acc. No. 18641.

Supernumerary and Accessory Ovaries

Wharton (1959) defines a supernumerary ovary as an extra gonad that is entirely separate from the normally placed one and appears to arise from a separate primordium. An accessory ovary is situated near the normal gonad and may be connected to it, giving the impression that it developed from a normal ovary. Accessory ovaries have been reported more frequently in women than supernumerary ovaries; neoplasms have been reported in accessory ovaries. Wharton (1959) stated that "accessory and supernumerary ovaries may not be as rare as we suppose" because of the relatively large number of reports of tumors in ectopic ovarian tissue. He also suggested that ectopic ovaries may become neoplastic more frequently than normal ones. Congenital defects of the uterine tube, uterus, kidney, and bladder have been found quite frequently in association with supernumerary and accessory ovaries in women.

I examined the reproductive tract from a 4-year-old, nulliparous, Guernsey heifer that was slaughtered because of anestrus associated with mucometra. Three ovaries were present on the left side and one on the right (Fig. 3.8). The left ovary that was located near the cranial part of the uterine horn measured 30 x 25 x 12 mm and contained a 17 x 12-mm corpus luteum. The middle gonad on the left measured 11 x 6 mm and the other left gonad measured 26 x 22 x 3 mm. Since the ovaries were connected, this was interpreted as a case of accessory ovaries. The left uterine horn consisted of two layers of smooth muscle and a mesonephric duct but no endometrium. The right ovary and right uterine horn appeared to be normal. The right uterine horn contained approximately 50 ml of mucoid material, and the cervix was filled with very tenacious mucus. The urinary system was not examined for malformations.

Lagerlöf and Boyd (1953) found one case of accessory ovaries during the postmortem examination of reproductive tracts from 5950 cows in Sweden. The cow had two ovaries on each side.

Small accessory ovaries in cattle are not uncommon and are usually overlooked. Accessory ovaries are located in the proper ligament of the ovary and are separated from the normal ovary by connective tissue (Fig. 3.9). Some are about 5 mm in diameter, while others are not visible on gross examination. I found accessory ovaries in five cows during the examination of 212 randomly selected reproductive tracts from slaughtered cows. Primary follicles and sometimes growing follicles are present. If the normal ovaries are surgically removed, the accessory ovary may become functional and form luteal tissue.

A direct extension of ovarian tissue into the proper ligament of the ovary for a distance of 2 to 3 cm occurs (Fig. 3.10) in some cows. This extension, and the presence of accessory ovaries, can be significant in physiologic studies involving surgical removal of ovaries. The compensatory activity of the remaining ovarian tissue can result in significant production of estrogen and progesterone.

The occurrence of estrus in the dog and cat after ovariohysterectomy may in some cases be due to the presence of an accessory ovary or of ovarian tissue that has extended into the proper ligament of the ovary. Three ovaries were found during a routine ovariohysterectomy of a cat (Anonymous, 1977). Two ovaries, which were about 1 cm apart, were present on the left side. Individually they were smaller than the single right ovary, but collectively the left ovarian

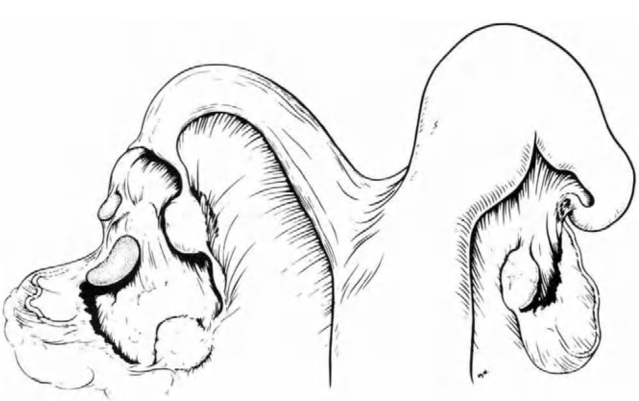

Fig. 3.8. Bovine reproductive tract with three ovaries on left. The stippled structures are cysts of the mesosalpinx. Acc. No. 9572.

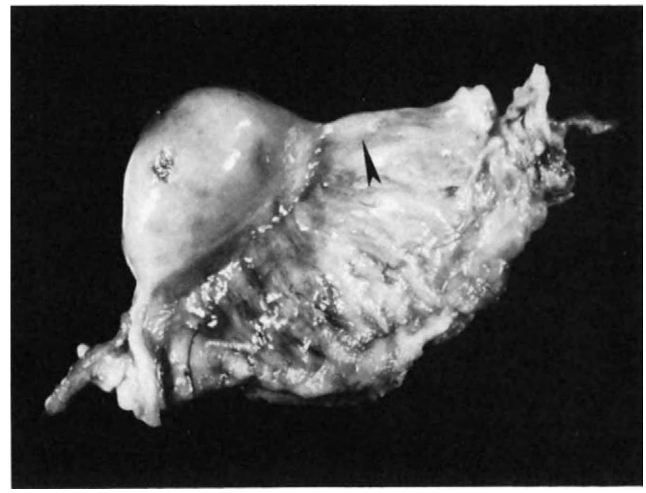

Fig. 3.9. Bovine ovary and small accessory ovary above arrow. Acc. No. 13504.

Fig. 3.10. Extension of ovarian tissue into proper ligament of bovine ovary. Acc. No. 15914.

tissue was more abundant. Arnbjerg (1980) reported a granulosa cell tumor that apparently developed in an accessory ovary of a cat.

Ovarian Agenesis

Agenesis of one or both ovaries rarely occurs in domestic mammals. Donald (1949) reported two cases of ovarian agenesis in an inbred litter of Large White pigs with kidney defects and kinky tails. Ovarian agenesis was bilateral in one and unilateral in the other. The kidneys were small or missing.

Ovarian Hypoplasia

Lagerlöf and Boyd (1953) defined ovarian hypoplasia as "a condition of incomplete ovarian development, wherein the affected ovary or part of the ovary completely lacks follicles." Ovarian hypoplasia, due to a germ cell deficiency, in domestic mammals has been studied most extensively in cattle of the Swedish Highland breed (SKB). This is a polled dairy breed from northern Sweden. The cattle are predominantly white with black or red ears and muzzle, and black or red spots on the sides of the body. Settergren (1961) found a very significant relationship between a deficiency of pigmentation of the ears and body and the occurrence of ovarian hypoplasia in SKB cattle.

Gonadal hypoplasia also occurs in SKB bulls. The condition was first recognized in bulls of the Swedish Highland breed as early as the end of the nineteenth century. By the mid-1930s the diagnosed incidence of ovarian hypoplasia in the cows in breeding herds was 17.3%. The adoption of control measures, initiated in 1936, resulted in the reduction of the incidence of ovarian hypoplasia to 7.3% for animals born during 1952 to 1954 (Lagerlöf and Settergren, 1961). Eriksson (1943) concluded that gonadal hypoplasia in the Swedish Highland breed is due to a recessive autosomal gene with incomplete penetrance. The narrow genetic base in the breed, as well as selection for white animals, allowed the defect to spread.

Settergren's (1964b) classic study of the ovaries of Swedish Highland cattle is recommended for the morphology of ovarian hypoplasia. He described three types of ovarian hypoplasia: total, partial, and transitional. In *total hypoplasia* the ovary was fusiform, had irregular longitudinal grooves on the surface, and contained no follicles. The average dimensions of totally hypoplastic ovaries were 18.8 mm long, 7.2 mm broad, and 6.8 mm thick. The average ovarian measurements of normal SKB heifers were 25.5 mm long, 18.8 mm broad, and 15.7 mm thick. With *partial hypoplasia* the uterine extremity of the ovary was affected most frequently and was small, wrinkled, and deficient in follicles. The tubal pole sometimes contained follicles and corpora lutea. The ovary with *transitional hypoplasia* was small and had a smooth surface and a firm consistency. Follicles and corpora lutea bulged from the surface in some cases. The average measurements of such ovaries were 19.8 mm long, 13.4 mm broad, and 11.3 mm thick. Thus they were larger than totally hypoplastic ovaries, the major differences being in breadth and width. Transitional ovarian hypoplasia was more difficult to diagnose clinically than total or partial hypoplasia and this probably contributed to the difficulty in controlling the condition.

Lagerlöf and Settergren (1961) conducted a survey of 1596 cases of ovarian hypoplasia. The frequencies of total unilateral or bilateral ovarian hypoplasia in SKB cattle were 87.5% left-sided, 3.6% right-sided, and 8.9% bilateral. In cases of total bilateral ovarian hypoplasia the uterus and mammary gland remain infantile and the pelvis is narrow.

Settergren (1964b) conducted quantitative investigations of the ovaries, after serially sectioning both gonads, from 48 SKB heifers and eight $3\frac{1}{2}$- to $8\frac{1}{2}$-month fetuses. The similarities between the basic structures of normal and hypoplastic ovaries included a normal surface epithelium, differentiation of cortex and medulla, and a normal rete ovarii. Deep longitudinal grooves were present in the ovarian cortex of both normal and defective fetuses. These grooves persisted in the hypoplastic ovaries of adult animals. The surface epithelium in the grooves was tall columnar but varied between squamous and columnar on the rest of the ovary. A lower surface epithelium was usually found in normal adults. Two of the fetuses had ovarian hypoplasia. The left ovary of a 6-month-old fetus weighed 0.057 g and the right ovary weighed 0.083 g. No oöcytes were present in the left gonad. The left ovary of an 8-month-old fetus weighed 0.133 g and the right ovary weighed 0.222 g. The cortex of the left ovary was very thin and contained only a few follicles. Many solid cords of cells, without oöcytes, were scattered throughout the cortex. Oöcytes were found in the medullary cords of the youngest fetuses.

In adult ovaries the tunica albuginea was similar in normal and hypoplastic ovaries. Anovular cords and anovular follicles were present in normal and hypoplastic ovaries but were more numerous in cases of hypoplasia and were directly related to the degree of underdevelopment. Medullary cords were present in all ovaries but were more numerous in hypoplastic ovaries. The medullary cords in defective ovaries were often arranged in nests surrounded by circular layers of connective tissue that sometimes contained "epithelioid cells" that were also present in the connective tissue around the rete ovarii. The rete ovarii occupied a relatively larger area in hypoplastic ovaries than in normal ovaries. The number of primordial follicles varied considerably from one area of the cortex to another in normal ovaries.

Settergren (1964a) found that the total number of primordial follicles in both ovaries of normal SKB heifers varied between 6800 and almost 100,000. Heifers with unilateral transitional hypoplasia had between 9500 and 43,400 primordial follicles and those with unilateral total hypoplasia had between 3100 and 41,600. He pointed out that some of the "normal" ovaries may have been defective. Disturbances in the development of follicles occurred when there was a very low number of follicles and the disturbances were most serious in those with the lowest number of follicles. Approximately 400 primordial follicles were necessary for ovulation to occur. When the follicle number was below 400, ovulation did not occur and the follicles luteinized. Interstitial gland formations occurred in the walls of atretic follicles when the number of primordial follicles was below 100. Interstitial glands were found in the medulla of some of the hypoplastic ovaries.

Ovarian hypoplasia occurs in other European breeds of cattle and in zebu cattle, but the incidence is much lower than in the Swedish Highland breed. Fincher (1946) described bilateral ovarian hypoplasia in three daughters from a cow that also had two normal daughters. The histology of the extremely small gonads was not reported.

I have seen a few cases of total, bilateral, ovarian hypoplasia in Holstein-Friesian heifers (Fig. 3.11). The histology of the ovaries was identical to that in Swedish Highland hypoplasia. Many more cases of testicular than of ovarian hypoplasia have been reported in breeds of cattle other than the Swedish Highland breed.

Low Germ Cell Resistance

Another type of genetic gonadal defect has been recorded as gonadal hypoplasia in a brief report by Lundgren (1972) in the Swedish Red and White breed (SRB) of cattle. Both sexes are affected. In a trial survey 30% of 110 daughters of one bull were suspected of having partial ovarian hypoplasia. I. Settergren (personal communication, 1973) believes that the condition is one of germ cell weakness in which excessive loss of germ cells occurs early in life. This differs from the classical ovarian hypoplasia in Swedish Highland cattle in which a deficiency or absence of germ cells occurs in fetuses as young as three to four months of age. Defective development of follicles and luteinization of follicles without ovulation occurs in affected SRB heifers with small ovaries.

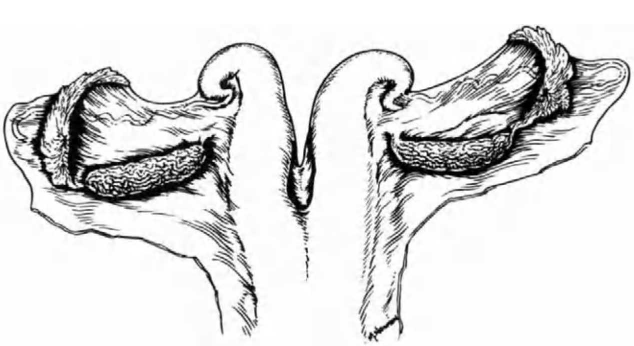

Fig. 3.11. Bilateral ovarian hypoplasia in a 15-month-old Holstein-Friesian heifer. Acc. No. 7428. (From Dobberstein *et al.*, 1985.)

Gonadal Dysgenesis

Cases of XY gonadal dysgenesis have been reported in heifers (Henricson and Akesson, 1967), and XO gonadal dysgenesis in horses, sheep, swine, and cats (Hughes *et al.*, 1975a; Zartman *et al.*, 1981; Nes, 1968; Norby *et al.*, 1974). The term gonadal dysgenesis means defective embryonic development of a gonad. It does not indicate whether the defective organ is an ovary or testis and does not identify the type of defect. It is a very broad term that includes gonadal aplasia, agenesis, and hypoplasia as well as hermaphroditic and streak gonads. In human pathology the term gonadal dysgenesis is usually used in reference to a streak gonad, which consists of a thin, white ridge of tissue in place of a normal ovary (Simpson *et al.*, 1976).

Henricson and Åkesson (1967) reported XY gonadal dysgenesis in two Swedish Red and White (SRB) heifers. One heifer had a feminine conformation and the other resembled a bull. The external genitalia of both heifers were normal, except for an enlarged clitoris in the feminine-appearing heifer. The teats and mammary glands were underdeveloped in both animals. The respective measurements of the almond-shaped ovaries in the feminine- and masculine-appearing heifers were, respectively: left, 33 x 16 x 7 mm; right, 38 x 14 x 7 mm; and left, 33 x 12 x 5 mm; right, 40 x 12 x 6 mm. Longitudinal grooves were present on all the ovaries. The number of follicles was reduced. Numerous anovular cords and follicles, as described by Settergren (1964b), were present in the cortex and medullary cords were in the medulla. No corpora lutea nor remnants of luteal tissue were mentioned. The karyotypes of the dam and two maternal half-sisters of one heifer were determined to be normal. The two affected heifers were not related.

Chapman *et al.* (1978) reported a case of XY gonadal dysgenesis in a 2-year-old, three-quarter Charolais heifer. The heifer had not shown estrus and had a masculine appearance, normal vulva, underdeveloped teats and mammary glands, and a narrow pelvic inlet. The vagina, cervix, and uterus were normal with the exception of a double external cervical os. The left gonad was oval, flattened, and measured 22 x 12 x 4 mm. A cystic uterine tube was present on the right side and a right gonad was not found. Anovular cords and follicles were present in the left gonad but no oöcytes were found. The dam and half-sister had normal female karyotypes.

XO-gonadal dysgenesis has been reported in the mare (Hughes *et al.*, 1975a,b; Chandley *et al.*, 1975; Hughes and Trommerhausen-Smith, 1977; Blue *et al.*, 1978; Bruere *et al.*, 1978; Trommerhausen-Smith *et al.*, 1979). The external appearance of affected mares is normal with the exception of a smaller than normal vulva. Many of the affected mares are smaller in height and weight than averages for their breeds. The condition has been diagnosed in many breeds, including Thoroughbred, Standardbred, Arabian, Quarter horse, Appaloosa, Belgian, and ponies. All the reported mares have been sterile and have lacked normal estrous behavior.

The cervix of mares with XO-gonadal dysgenesis is flaccid and open and the uterus is small. The hypoplastic ovaries are smooth and firm and vary in weight from 0.25 to 5.7 g. The gonads consist of ovarian stroma and occasionally a few atretic follicles. Blue *et al.* (1978) recorded "the presence of a number of presumptive atretic Graafian follicles and a discrete area of functional luteal tissue in the right ovary of one case." Hughes and Trommerhausen-Smith (1977) reported that "Plasma LH levels were significantly greater than those found in normal dioestrous mares (2.4 to 20 ng/ml compared to 0.4 to 1 ng/ml) in four 63,XO mares." Bruere *et al.* (1978) suggested that "there may be an undisclosed number of XO and possibly XO/XX mosaic mares which may not be entirely sterile but may be characterized by either reduced fertility or embryonic loss." They also suggested that "Sex chromosome abnormalities may be quite a common cause of sterility in the mare."

The following karyotypes have been found in mares with severe ovarian hypoplasia: 63,XO; 63,XO, 64,XY; 63,XO, 64,XX; 65,XXX; 64,XY; or autosomal deletion (64, XX? del 2 q−). The 63,XO is the most common karyotype found in association with gonadal dysgenesis in the mare.

Ectopic Adrenal Cortical Tissue

Ono *et al.* (1969) reported the presence of adrenal cortical nodules around the ovaries of 169 (59%) of 271 mares. Most of the adrenal nodules were located "at the junctional portion of the ovarian medulla and mesovarium, on the side of the plica suspensoria ovarii in single or plural number." The yellow-white or orange-yellow nodules of tissue varied in size from pinhead to 2.5 cm in diameter. Histologically, the zona glomerulosa and fasciculata are usually well defined (Fig. 3.12). Degeneration and calcification of the central portions had occurred in some of the larger nodules. The highest incidence of adrenal cortical nodules was found in diseased, pregnant mares (93.9%). This suggests that the combined stresses of pregnancy and disease cause hyperplasia of the adrenal rests. Since such a high incidence was found in such mares, it would appear that the majority of mares have ovarian adrenal cortical tissue in and around the ovaries.

Kenney and Ganjam (1975) reported a 15-g ectopic adrenal cortical mass attached to one ovary of a 14-year-old Thoroughbred mare. Hormone analysis of the tissue revealed the presence of progesterone (11.4 ng/g), 20-hydroxyprogesterone (9.5 ng/g), and 17-hydroxyprogesterone (55.2 ng/g).

Altera and Miller (1986) found parovarian nodules of adrenocortical tissue in the broad ligament, within 1 to 4 cm of the ovary, in 17 cats. The nodules were usually single, 2 to 5 mm in diameter, smooth, firm, and gold to tan. In a subsequent survey of the reproductive tracts of 499 cats undergoing routine ovariohysterectomy, they found 11 (2.2%) cats with parovarian nodules of adrenocortical tissue.

Microscopic nodules of adrenal tissue may be found near the epoöphoron and in the mesosalpinx. Adrenal medulla does not occur in the nodules. Ovarian adrenocortical tissue has been found in the mesovarium and/or mesosalpinx of all species of domestic mammals.

Ovarian Tissue in the Adrenal Gland

Wong and Warner (1971) reported the presence of ectopic ovarian stroma in the adrenals of middle-aged women. They stated that "The foci of ectopic

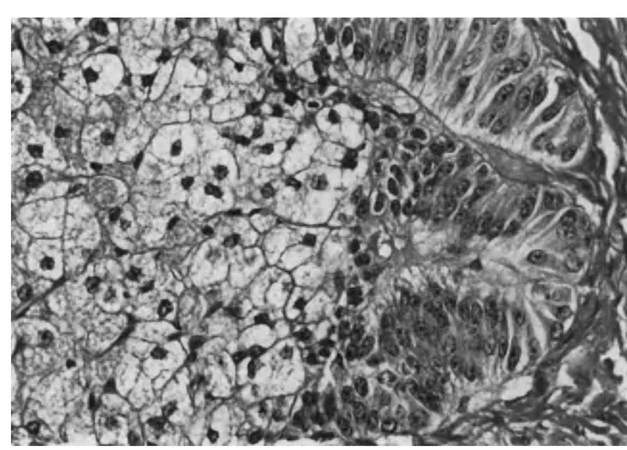

Fig. 3.12. Ectopic adrenal cortical tissue that was located on the surface of an equine ovary. ×385. Acc. No. 19304.

ovarian stroma are generally attached to the adrenal capsule and are made up of thecal elements, similar to those observed in the cortex of the ovary or in thecomas, for which we have applied the term 'thecal metaplasia'. . . . This ectopia of adrenal tissue is believed to be due to the close anatomical relationship between the adrenal cortex and the gonad in embryological development; both primordia arise in the region of the urogenital ridge."

Fidler (1977) stated that "Wedge-shaped microscopic nodules resembling ovarian stroma or theca were found in the adrenal cortices of 14 women. Thirteen of the women were postmenopausal, and one had ovarian stromal hyperplasia. The lesions were frequently multiple and bilateral and were almost always located just beneath the adrenal capsule."

I have seen ovarian stromal tissue in a bovine ovary.

Fig. 3.13. Adhesions covering left ovary of a cow. Acc. No. 454.

Ovarian Hemorrhage

Intrafollicular hemorrhage occurs frequently in atretic follicles in young calves but rarely in atretic follicles in cows. The amount of hemorrhage that occurs during ovulation varies in different species. In the cow a small blood-filled cavity in the corpus luteum will be present for only a few days following ovulation. The mare develops a large corpus hemorrhagicum following ovulation. According to Hughes (1974), hematomas forming within the ovulation site in the mare may be as large as 27 cm and can persist for several months without affecting the estrous cycle. Fatal hemorrhage can occur from the corpus hemorrhagicum.

Hemorrhage and Adhesions following Enucleation of Corpora Lutea in Cattle

Dawson (1961) reviewed the literature on corpus luteum enucleation in the cow. The technique has been used frequently in the past for inducing estrus in cattle. Most cows survived enucleation of a corpus luteum and remained fertile, otherwise the procedure would have been discontinued long ago. According to Dawson (1961), "The simple operation of corpus luteum enucleation in the cow has probably been performed for centuries all over the world."

The adverse effects of corpus luteum enucleation in the cow include fatal hemorrhage, periovarian adhesions (Fig. 3.13), ovarian abscesses, and cystic follicles following repeated enucleations at short intervals. The incidence of fatal hemorrhage has been reported to vary from 1 : 1000 to 1 : 9000 (Teige, 1955) and from 1 : 300 to 1 : 500 (Roberts, 1971). A relationship may exist between the level of milk production and the tendency toward fatal hemorrhage with the most severe hemorrhage occurring in the highest producers. Stormorken and Teige (1953) found that cows that had serious bleeding following enucleation of a corpus luteum had only one-third the normal level of prothrombin.

Heckhausen (1950) determined the amount of free blood in the abdominal cavity of cows that were slaughtered 2 to 6 hours following enucleation of the corpus luteum. In a series of 25 cows that had normal estrous cycles, free blood in the peritoneal cavity varied from less than 1 liter in 3 cows to 3 or more liters in 15 cows. Ovarian hemorrhage had ceased at the time of slaughter in all cases.

Thirty-two cows that had been diagnosed as having persistent corpora lutea experienced less hemorrhage. Two had 1 liter and the rest had 1 1/2 liters of blood in the peritoneal cavity. In the light of our present knowledge, it appears that these cows did not have persistent corpora lutea but were experiencing silent or subestrous cycles. The most severe hemorrhage occurred in pregnant cows and in those with pyometra. Four to 7 liters of blood were found in these cases and hemorrhage continued until the time of slaughter in many of the animals. This evidence indicates that the cows that actually have persistent corpora lutea, that is, those that are pregnant, have pyometra, etc., are much more likely to experience profuse hemorrhage following enucleation of luteal tissue. In the cases of persistence of the corpus luteum the luteal tissue is more firmly embedded in the ovary and has a more highly developed blood supply than the cyclic corpus luteum. Rupture of ovarian cysts is not followed by as severe hemorrhage as the enucleation of corpora lutea.

Extruded corpora lutea remain indefinitely, either attached to a pelvic or peritoneal organ (Fig. 3.14) or as free-floating bodies in the peritoneal cavity. Large star-shaped scars remain on the surface of the ovary following enucleation of the corpus luteum. On careful examination the number of large scars and remnants of corpora lutea in the abdominal cavity can be correlated. The remnant of the corpus luteum resembles a lima bean in shape and size. Care must be taken to differentiate these bodies from pedunculated lipomas that have become detached. On histologic examination, the ghostlike remnants of luteal cells can be identified in an extruded corpus luteum and fat cells in a detached lipoma. The mass of necrotic luteal cells is surrounded by a fibrous tissue capsule.

The enucleation of corpora lutea in some cows with pyometra results in the formation of dense adhesions around the ovaries and the development of ovarian abscesses. Schneider *et al.* (1979) reported the effects of one to four enucleations of corpora lutea or manual rupture of ovarian cysts in 59 virgin heifers. Periovarian adhesions formed in 23 (39%) of the heifers. In a control group of 65 heifers, 9% had slight intrabursal adhesions (ovulation tags).

Purse and Wickersham (1969) reported that "Successive enucleation of luteal tissue at day 10 postestrus resulted generally in the formation of increasingly more cystic structures, progressing from normal corpora lutea to cystic corpora lutea to luteinized follicles with ovulation failure." McKay and Thompson (1958) and Foote *et al.* (1959) reported a high incidence of cystic ovaries following enucleation of corpora lutea. The latter also reported an increase in the incidence of double ovulation after enucleation of corpora lutea.

Many sound reasons can be given for discontinuing the practice of enucleating corpora lutea in cattle. In the majority of cases the procedure is used to induce estrus in cases of so-called "silent" estrus. The vast majority of these cows are experiencing estrus that is not being detected. More effort should be devoted to improvement of management, record keeping, and the detection of estrus. The possibility that subestrus may have a genetic basis should also be considered. If it is necessary to induce estrus, prostaglandins can be used without the traumatic effects of enucleation of luteal tissue. Corpora lutea are seldom enucleated in cattle in Sweden and the incidence of dense ovarian adhesions is extremely low in contrast to countries such as the United States, where a large percentage of the dense ovarian adhesions found in slaughtered cattle are sequelae of luteal enucleation.

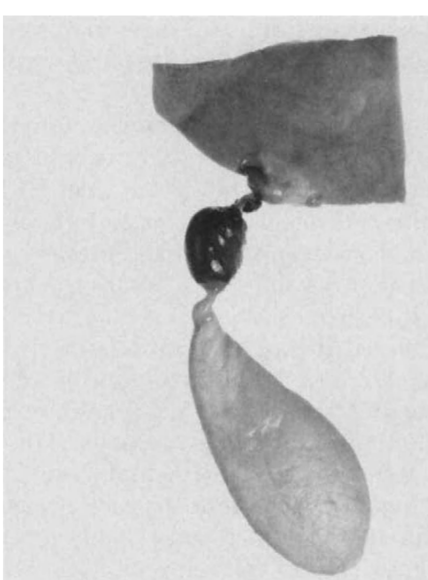

Fig. 3.14. Extruded bovine corpus luteum attached to liver. Acc. No. 730.

Ovulation Tags

Small clots of blood and follicular fluid attach to the surface of the ovary and the proper ligament of the ovary following ovulation and gradually become transformed into fine strands of fibrous tissue (Fig. 3.15). These strands of tissue frequently extend from the ovary and across the ovarian bursa to the uterine tube and mesosalpinx, forming weblike adhesions. They are easily broken during per rectal examination of the uterine tubes and do not interfere with fertility. Hartman (1944) described ovulation tags in the rhesus monkey and suggested that they form on strands of drawn-out liquor folliculi. The lesion is composed of fibrin, proliferating capillaries, and leu-

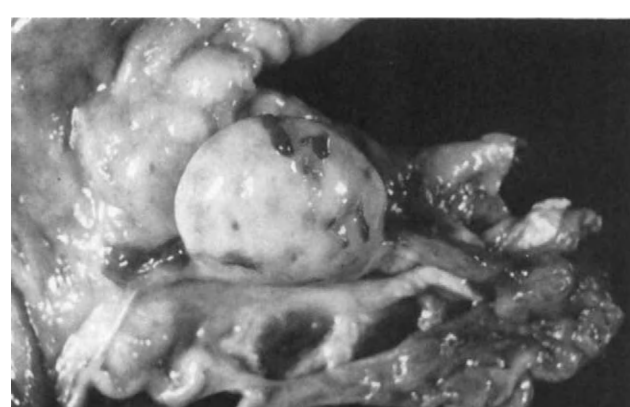

Fig. 3.15. Ovulation tags on proper ligament and surface of bovine ovary. Acc. No. 16313.

kocytes. Neutrophils are numerous at first, but these are gradually replaced by lymphocytes, macrophages, and plasma cells. Peritoneum covers the tags and is infolded into the granulation tissue. The proliferating peritoneal tissue sometimes resembles a mesothelioma histologically. As the inflammatory lesion gradually subsides only fine strands of fibrous tissue remain. Many of these apparently disappear because fine ovarian adhesions seem to be more common in heifers than they are in mature cows. These adhesions have not been observed in sexually immature animals, which is as expected.

Vascular Lesions

Degenerative and inflammatory lesions have been observed in the small arteries of the theca interna of atretic follicles in postpartum heifers. The incidence and significance of these vascular lesions are unknown. Mucoid degeneration of the intima and hyalinization of the media of large arteries supplying the corpora lutea of pregnancy occur during the postpartum period. Similar lesions occur in the arteries of the caruncular stalk during uterine involution.

Thrombosis of the ovarian vein occurs in the medulla of the bovine ovary. The condition appears to occur more frequently in zebu cattle than in European breeds. The thrombus may become large enough to cause virtual destruction of the ovary. In women it is considered to be due to postpartum, ovarian thrombophlebitis (Lotz *et al.*, 1966).

Varicose veins develop on the surface of the ovary (Fig. 3.2) in aged mares and cause gradual destruction of the zona parenchymatosa (cortex). The large ovarian veins of the mare are prone to develop varicosities because they are located peripherally instead of centrally as in other species. Thrombi form in some cases. These become mineralized and may detach from the vessel wall to remain as free-floating, spherical, firm bodies in the dilated veins. They can be palpated on the ovary as firm, slightly movable bodies.

Oöphoritis (Ovaritis)

Eosinophils occur in recently formed corpora lutea in cattle (McNutt, 1924; Moss *et al.*, 1954; Cupps *et al.*, 1959), sheep, and swine (Corner, 1919, 1921). Brown and Nellor (1968) reported that in swine "estrogen secretion by the ovary, as estimated by changes in genital tract tissues, can be directly correlated with the appearance of eosinophilic granulated cells within ovarian tissues. . . . Eosinophilic granulated cells were observed in the thecal layers of secondary, tertiary and atretic follicles and in the connective tissue surrounding and penetrating recently formed corpora lutea. Ovarian eosinophilic granulated cells are not of immediate blood origin but arise from undifferentiated mesenchymal cells. . . . Whereas the appearance of eosinophilic granulated cells of the genital tract are coincident with increased bactericidal activity, a physiological function for ovarian eosinophilic is not obvious."

Summers *et al.* (1974) observed mild, interstitial oöphoritis in Brahman and Santa Gertrudis cattle in Australia. The lesion consisted of perivascular accumulations of lymphocytes and some plasma cells in the ovarian medulla. The lesion was seen in 14 (73.7%) of 19 infertile Brahman and Brahman-cross cattle from a herd that had prenatal losses in all stages of gestation. Four (25%) of 16 infertile Santa Gertrudis cows and 10 (23.8%) of 42 control cows, which had been slaughtered for reasons other than infertility, had interstitial oöphoritis. They concluded that "Although the overall situation was compatible with infection, no correlation was apparent with the common bacterial, viral or protozoal diseases."

Wrathall and Mengeling (1979) found inflammatory lesions in the corpora lutea of gilts that were infected experimentally with porcine parvovirus (PPV). Fertilized eggs were cultured for approximately 21 hours in a medium containing PPV and transferred to the uterus of gilts that were seronegative to PPV. The gilts were killed on Day 10 of pregnancy. They reported that "the corpora lutea contained numerous foci of mononuclear inflammatory cells, mainly lymphocytic in type but with some plasma cells, and these foci were closely associated with the centripetal vascular network. Occasional foci were also seen in the thecae."

Parsonson *et al.* (1981) reported that cows infected with Akabane virus at the time of insemination developed multifocal necrosis and inflammatory cell foci in luteal tissue. The lesions were noted as early as 4 days following inoculation. At this time, the areas of necrosis were accompanied by accumulations of macrophages and small foci of lymphocytes. By Day 10 the areas of necrosis were heavily infiltrated by lymphocytes and plasma cells. By Day 50 there was no evidence of ovarian damage.

Bolin *et al.* (1985) reported the effects of intrauterine inoculation of sows with pseudorabies virus within 6 hours after natural mating. The virus was isolated from the reproductive tract up to Day 14 postinoculation. "Lesions in the reproductive tract consisted of multifocal to diffuse lymphohistocytic vaginitis and endometritis, and lymphoplasmacytic aggregates in the corpora lutea" (Bolin *et al.*, 1985).

Miller and Van Der Maaten (1984) reported the presence of focal necrosis and lymphocytic foci in corpora lutea and other ovarian tissue in heifers given infectious bovine rhinotracheitis virus by intrauterine inoculation on Day 1 after natural mating. The heifers were killed 4 to 14 days postinoculation.

Severe oöphoritis is comparatively rare in cattle in areas free of tuberculosis and brucellosis. Tuberculosis of the bovine ovary starts as small, red, granular lesions on the serosa. The ovary becomes invaded through the point of rupture of a vesicular follicle. As the disease progresses the ovary becomes embedded in granulation tissue and adherent to the uterine tube. Tuberculous oöphoritis is almost always accompanied by salpingitis and metritis. The lesions consist of granulomas containing numerous epithelioid cells and Langhans-type giant cells containing acid-fast organisms.

Brucellosis in swine produces ovarian serosal granulomas that resemble tuberculous lesions histologically. Brucella-infected cattle frequently develop chronic salpingitis and adhesions between the uterine tube and ovary.

Ovarian abscesses in cattle are rare and may develop secondary to severe cases of postpartum metritis and pyometra. Couto and Megale (1959) found one ovarian abscess during the postmortem examination of 1300 bovine genitalia in a slaughterhouse survey. *Actinomyces pyogenes (Corynebacterium pyogenes)*, which is the usual abscess-producing organism in the cow, was isolated from the exudate. Al-Dahash and David (1977) did not find any ovarian abscesses during the examination of 8071 reproductive tracts from slaughtered cattle.

The enucleation of a corpus luteum in a cow with pyometra occasionally results in the development of an ovarian abscess. The crater remaining in the ovary following the removal of a corpus luteum provides a focus for the growth of bacteria that are invariably present in the uterine tubes of cows with pyometra. Hormone therapy, rather than corpus luteum enucleation, should be used for treating pyometra in the cow.

Hartman *et al.* (1964) and Hirth *et al.* (1966) demonstrated that *Mycoplasma bovis* is capable of producing severe salpino-oöphoritis in heifers. They inoculated broth suspensions of *M. bovis* into the uterus and artificially inseminated heifers with semen containing approximately 1.0×10^7 *M. bovis* organisms per 1 ml. Infected heifers developed suppurative endometritis, salpingitis, and peritonitis involving the cranial portions of the uterine horns, uterine tubes, and ovaries. The lesions were severe enough to cause sterility in some cases. Four of 12 heifers, which were inseminated with semen containing live mycoplasma organisms, failed to conceive after as many as five inseminations. It is quite possible that some of the severe cases of chronic salpino-oöphoritis that are seen in cattle throughout the world are due to chronic mycoplasma infection. In long-standing cases of salpino-oöphoritis the ovaries and uterine tubes become buried in dense fibrous tissue.

The migration of *Strongylus edentatus* larvae to the ovary of the mare produces dense adhesions between the ovulation fossa and uterine tube. The lesions are usually confined to the surface of the ovary but occasionally larvae penetrate the ovary, causing necrosis, hemorrhage, and a granulomatous reaction. Eosinophils are numerous in early stages of the reaction but are less common in more chronic lesions, where multinucleated giant cells are prominent.

Drudge *et al.* (1956) reported a third stage larva of *Gasterophilus intestinalis* in a 3-cm cyst of the left ovary of a Thoroughbred mare. The bot was surrounded by blood and fibrinous material. They stated that "There was no opening between the cyst and the surface of the ovary. No ruptures or perforations were found in the stomach and intestines." They were unable to suggest the route of infection.

Progressive and Regressive Processes

The ovaries of most domestic mammals become progressively larger with increasing age. The increase in size is due to the accumulation of fibrous tissue resulting from degeneration of corpora lutea and to vascular lesions following repeated pregnancies. The ovary of the aged sow and bitch becomes very lobulated with advancing age.

Unilateral ovariectomy results in compensatory hypertrophy of the remaining ovary. Marked hypertrophy of an accessory ovary in the cow occurs following surgical removal of both normal ovaries. The increase in size of accessory ovaries is due to the growth of follicles and formation of luteal tissue. The nature of the compensatory changes in the ovary has been reported in swine (Short *et al.*, 1968), sheep (Mallampati and Casida, 1970), and cattle (Saiduddin *et al.*, 1970).

Complete cessation of ovarian activity, as occurs in menopausal women, is not recognized in domestic mammals. A continual loss of oöcytes and decrease of fertility occur with advancing age, but ovarian activity continues.

Ovarian atrophy may occur as a result of any severe, chronic, debilitating disease. A much more severe stress is required to stop ovarian function in European breeds of cattle than in zebu cattle. After the start of the dry season, the ovaries of zebu cattle become inactive and estrous cycles cease as a result of nutritional deficiencies. The ovaries decrease in size owing to the absence of large follicles and corpora lutea. In some atrophic zebu ovaries the medulla is dark brown in color from the accumulation of pigment in macrophages. Ovarian activity commences after the onset of the rainy season.

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Chapter 4

Cysts in and around the Ovary

Cysts in the Ovary
- Normal Mature Follicles
- Atretic Follicles
- Cystic Follicles
- Luteinized Follicles
- Cystic Corpora Lutea
- Epithelial Inclusion Cysts
- Cysts of the Subsurface Epithelial Structures
- Cystic Rete Ovarii
- Single Large Cyst

Cysts around the Ovary
- Cysts of Mesonephric Tubules and Ducts
- Cystic Accessory Uterine Tubes and Accessory Funnels
- Tubo-ovarian Cysts
- Cystic Ovarian Bursa

Bibliography

When the term "cystic ovary" is used, one usually thinks of the follicular cyst, but this is neither the most common nor the most important ovarian cyst in all species of domestic mammals. Sixteen different types of cysts occur in and around the ovary. The incidence and clinical significance of the various types of cysts vary among the different species of domestic mammals. Cysts in and around the ovary are classified according to their origin as shown in Table 4.1.

Cysts in the Ovary

Normal Mature Follicles

It is essential for both the clinician and the pathologist to know the size of normal mature follicles in the various species of domestic mammals because one of the criteria for diagnosing a cystic follicle is the size of the cyst. Follicles larger than those listed in Table 4.2 are considered to be cystic based on clinical or gross postmortem examination. Histologic examination of the surgical or postmortem specimen should be done to verify or refute the gross diagnosis.

Atretic Follicles

Follicular atresia is a normal physiologic process that starts during fetal development and continues throughout life in domestic mammals. The following references concerning follicular atresia are recommended: cow: Rajakoski (1960); Marion *et al.* (1968); sow: Wrathall (1980); ewe: Brand (1970); Hay *et al.* (1976); O'Shea *et al.* (1978); mare: Kenney *et al.* (1979); and bitch: Anderson and Simpson (1973); Stott (1974).

Cow. Rajakoski (1960) described four types of follicular atresia in cattle. The first type of atresia (atresia with primary oöcyte degeneration without hyalinization in the zona pellucida) occurs in the primordial and the smallest of the growing follicles. The degenerative changes start in the oöcyte and consist of chromatolysis, disappearance of the nuclear membrane, shrinkage of cytoplasm, and penetration of the zona pellucida by macrophages. The degeneration of the oöcyte is followed by degeneration of the granulosa cells and disappearance of the entire follicle into the cortical stroma.

The second type of follicular atresia (atresia with primary oöcyte degeneration with hyalinization of the zona pellucida) occurs in growing follicles with a well-developed zona pellucida and in vesicular follicles up to 1 or 2 mm in diameter. The first signs of atresia are observed in the oöcyte and are similar to those in the first type of atresia. The zona pellucida increases in thickness and becomes opaque and hyalinized. The cytoplasm of the granulosa cells decreases and the cell outlines become indistinct. It appears that this type of degeneration occurs over a long period of time.

The third type of follicular atresia (obliterative atresia with primary follicular wall degeneration) occurs in vesicular follicles from 1 to 6 mm in diameter. Degeneration occurs first in the mural portion of the granulosa while mitotic figures are still evident in the cumulus and theca. Mitotic activity then ceases and thecal connective tissue cells extend into the antrum

Table 4.1
Classification of Cysts by Origin

Origin	Type of cyst
In the Ovary	
Follicle	1. Normal vesicular follicle
Follicle	2. Normal atretic follicle
Follicle	3. Cystic follicle
Follicle	4. Luteinized follicle
Follicle	5. Cystic corpus luteum
Surface epithelium	6. Epithelial (germinal) inclusion cyst
Subsurface epithelial structures (SES)	7. SES cyst
Rete ovarii	8. Cystic rete ovarii
Self-destructing, cystic granulosa cell tumor	9. Single large cyst
Around the Ovary	
Mesonephric tubules	
Cranial mesonephric tubules	10. Cystic epoöphoron
Caudal mesonephric tubules	11. Cystic paroöphoron
Mesonephric duct	12. Mesonephric duct cyst
Paramesonephric appendix	13. Cystic accessory funnel
Appendix vesiculosa (hydatid of Morgagni)	14. Cystic accessory uterine tube
Uterine tube and ovary	15. Tubo-ovarian cyst
Uterine tube, mesosalpinx, and ovary	16. Cystic ovarian bursa

to eventually obliterate the space. Follicular fluid is lost, the cumulus disappears, and the oöcyte degenerates, leaving an opaque zona pellucida. The theca becomes hyalinized. The end product of degeneration is called a corpus atreticum; it is seldom larger than 1 mm.

The fourth type of follicular atresia (cystic atresia) differs from obliterative atresia in that the primary loss of follicular fluid does not occur. The granulosa cells degenerate. The theca interna becomes atrophic and is poorly delineated from the ovarian stroma. Follicular liquor is lost only after complete degeneration of the follicular wall. A hyaline membrane does not form in the theca as in the third type of atresia. The antrum gradually decreases in volume after being enclosed in the connective tissue capsule. According to Rajakoski, "Regression in cystic atresia, as the name would suggest, follows much the same course as in a so-called cystic Graafian follicle."

Table 4.2
Size of Normal Mature Follicles

Queen	2 to 3 mm	Foster and Hisaw (1935)
Bitch	5 to 8 mm	Concannon *et al.* (1977)
Doe (goat)	8 to 10 mm	Harrison (1948)
Ewe	8 to 10 mm	Grant (1934)
Sow	8 to 10 mm	Burger (1952)
Cow	16 to 19 mm	McNutt (1924)
Mare	30 to 70 mm	Arthur (1958)

Mare. Kenney *et al.* (1979) studied morphological and biochemical correlations of vesicular follicles in the mare during estrus. They reported that "A seemingly important stage in maturation appeared to be at 3 cm in diameter since follicular oestrogens and androgens underwent a three-fold increase in concentration at that size." They presented evidence to suggest that estrogens are antiatretogenic, but that a drop in estrogens is not the cause of atresia because it commenced when estrogen levels were high. They concluded that "Follicular atresia in the mare appears to be a gradual process of which the initiating cause remains unknown."

Bitch. Atresia of primary follicles may start with degeneration of the oöcyte but with persistence of the granulosa cells. This results in the formation of anovular follicles. These may form a chain of small cysts parallel to the ovarian surface in the periphery of the cortex.

A portion of the granulosa cells persists during atresia of vesicular follicles. The persisting granulosa cells proliferate in the canine ovary and extend into the surrounding stromal tissue. They form straight or tortuous cords of spindle-shaped cells arranged perpendicular to the surrounding connective tissue.

These structures were called granulosa cell cords by Andersen and Simpson (1973) and granulosa cell islands by Stott (1974).

Cystic Follicles

Cystic follicles occur most frequently in the cow and sow and are an important cause of infertility and sterility in these species. Cystic follicles occur less frequently in the bitch and queen and rarely in the ewe, doe (goat), and mare.

Cow. Cystic follicles in dairy cattle occur most frequently in the early postpartum period. Morrow *et al.* (1966) reported the results of a study of 357 postpartum cycles in 139 dairy cows. The cows were examined by per rectal palpation of the reproductive organs twice weekly for 60 days postpartum. A follicle larger than 2.5 cm in diameter on three successive examinations in a 10-day period was considered to be cystic. Normal mature follicles in the cow are rarely larger than 19 mm. Statements placing the minimum size of cystic bovine follicles at 2.5 cm are in clinical reports and are erroneous. The mean occurrence of cystic follicles in the 139 cows during the 60-day postpartum period was 12.3%. Cows that had parturient and postparturient diseases (abnormal cows) had significantly higher incidence (23.4%) of cystic follicles than normal cows with an 8.3% incidence. Fifteen percent of the normal cows developed cystic follicles at the first postpartum estrus as compared to 38% of the abnormal cows. The incidence of cystic follicles decreased from the first to the second and from the second to the third estrus. The frequency of occurrence of cystic follicles in the abnormal cows declined from 38% at first estrus at 8% at the second estrus. The difference was highly significant ($P < 0.005$). The decline in frequency of occurrence of cystic follicles in all cows was from 20% at the first estrus to 7% at the second estrus. The intervals from parturition to first estrus were 37 days in cows with cystic follicles as compared to 20 days in cows with normal follicular development and ovulation. The 17-day difference was highly significant ($P < 0.01$). The longer intervals in cows with cystic follicles resulted because approximately 82% of these cows did not show estrus. Approximately 48% of the cows with cystic follicles recovered spontaneously. Cows were treated when cystic follicles persisted until 60 days postpartum or when nymphomania was present.

Garcia and Larsson (1982) recorded the occurrence of follicular cysts in cows during the postpartum period. They stated that "For Swedish conditions the incidence of cows with cystic ovarian structures was high (14.8%)." However, only 2.2% of cows needed hormonal treatment for resumption of cyclic ovarian activity.

DeLange (1950) conducted a thorough study of the effects of withholding a group of 25 beef heifers from breeding until they were 4 to about 6 years old. Twelve of the animals developed follicular cysts. Eight had never been bred and only two had conceived prior to the development of follicular cysts. Signs of nymphomania were observed in ten cases, whereas the onset of follicular cysts was accompanied by anaphrodisia in the remaining two. Anaphrodisia followed all cases with nymphomaniac signs, except for one cow that was slaughtered a month after the initiation of clinical signs. The duration of nymphomania preceding anaphrodisia varied from 2 to 26 months. The longer the signs of nymphomania persisted, the more pronounced the signs of masculinity became. These signs included coarse head and shoulders, relaxation of the sacrosciatic ligaments, elevation of the tail head, depression of the back in the lumbar region, deep bull-like voice, and mounting other animals but refusing to stand for coitus. During anaphrodisia, the animals became quite passive and no further alterations occurred in their physical appearance.

In a study of 352 cases of cystic ovaries in cattle, Roberts (1955) "found that the cyst or cysts were located on the left ovary in 80 (23%), on the right ovary in 117 (33.2%) and on both ovaries in 154 (43.8%) of the cases." In 265 cases where the history and signs are known, 195 (73.6%) of the cows showed signs of nymphomania while 70 (26.4%) showed anestrus over an extended period. More recent evidence indicates that the incidence of anestrus, associated with follicular cysts, is higher than the 26% reported by Roberts. The occurrence of anestrus, associated with cystic follicles, during the 60-day postpartum period has been reported to be 86% (Marion and Gier, 1968) and 65% (Morrow, 1971). The increased detection of anestrus, associated with follicular cysts, is apparently due to more frequent and diligent examination of cattle during the 15- to 60-day postpartum period, and also because (1) cystic follicles occur most frequently in the early postpartum period and (2) the majority of cows that develop follicular cysts during this time do not show signs of estrus (Erb and White, 1981).

Garm (1949a), DeLange (1950), Jubb and Kennedy (1970), and Al-Dahash and David (1977a,b,c) described the gross and microscopic lesions associated with follicular cysts in cattle. The most detailed report of the pathologic changes was presented by DeLange. Follicular cysts start to develop early in estrus when release of luteinizing hormone from the adenohypophysis is faulty. The mature follicle fails to ovulate and continues to increase in size. The early stage of the development of the syndrome is usually characterized by the presence of a single cyst that is larger than a normal follicle. Most clinical investigators have used the diameter of 2.5 cm as the size for differentiating normal follicles from cystic follicles on per rectal examination. However, normal bovine vesicular follicles seldom exceed 2 cm in diameter.

In cystic degeneration of mature follicles, degeneration of granulosa cells occurs first, followed by degeneration of the oöcyte and the theca interna. The granulosa cells undergo pyknosis and karyorrhexis and slough into the cyst cavity. The theca interna cells undergo pyknosis with subsequent fibrosis of the cyst wall. Luteinization of the theca interna, when it occurs, varies from small isolated patches to thick crescents that are usually located at the base of the cyst deep in the ovary. Al-Dahash and David (1977b) found luteinization in 111 (22.84%) of 486 cysts in an abattoir survey. The partial luteinization of the cyst wall appears to occur predominantly in the theca interna, but may occur in the granulosa.

Cows with chronic cystic follicular degeneration may have lesions in a number of extraovarian organs, including the uterine tubes, uterus, cervix, vagina, vulva, mammary glands, adrenals, and pituitary. The mucosa of the uterine tubes becomes thick and edematous. In reference to the epithelium of the uterine tube DeLange (1950) reported that "In a number of cases similar basal vacuoles are present, as observed at two days post-oestrum. In the former cases, however, the vacuolation is more extensive."

The endometrium becomes hyperplastic with dilatation of the endometrial glands in nymphomaniac cows with persistent follicular cysts. The cysts are multiple, evenly scattered throughout the endometrium, and vary in size from less than 1 mm to more than 10 mm in diameter. Numerous small cysts give the endometrium a granular appearance. Abundant mucus may be evident in the cystic glands. The endometrial stroma is edematous.

Atrophy of the myometrium and endometrium may follow cystic hyperplasia of the endometrium. In these cases, mucoid or watery material accumulates in the uterine lumen. This sequence of events may start with the onset of cystic follicular degeneration accompanied by anestrus or may follow a prolonged period of nymphomania. The extreme thinness of the atrophic uterine wall is a characteristic feature of hydrometra associated with chronic cystic follicular degeneration.

In cases of functional follicular cysts (those producing estrogen), the cervical canal is usually dilated, allowing fluid to escape from the uterus. The mucosa of the cervix consists of tall columnar cells similar to those seen at 2 days postestrum in normal cows. Edema and congestion of the stroma occur. Squamous metaplasia may occur at the base of the crypts, especially in the first and second cervical rugae. The metaplasia occasionally results in the formation of small inclusion cysts lined by stratified squamous epithelium.

In nymphomaniac cows, the vaginal mucosa is edematous and may be thrown up into folds. Cystic mesonephric (Gartner's) ducts are present in some cases. The cystic distention appears to be secondary to squamous metaplasia of the ductal epithelium.

The vulva becomes edematous when the cysts are producing estrogen and the clitoris may become enlarged in long-standing cases. Chronic edema of the vulva results in fibrosis and marked enlargement of the vulva in long-standing cases. The superficial epithelial cells may be cornified. The major vestibular (Bartholin's) glands become cystic as a result of squamous metaplasia and occlusion of the ducts. Abundant mucus may flow from the genital tract following vigorous palpation of the uterus.

A remarkable degree of development and secretory activity of the mammary glands in cows with chronic cystic ovarian degeneration is possible. The secretion varies from a small to moderate amount of yellow, watery fluid to thick, creamy material resembling colostrum.

The onset of cystic follicular degeneration begins at the time of estrus and is related to abnormal pituitary function. In normal cows, the delta cells of the adenohypophysis degranulate early in estrus, whereas the delta cells fail to degranulate in cows that do not ovulate and subsequently develop follicular cysts (Jubb and McEntee, 1955; McEntee and Jubb, 1957). The pituitary gland enlarges significantly in cows with persistent follicular cysts (Garm, 1949a).

Significant enlargement of the adrenal glands occurs in cows with cystic follicular degeneration (Garm, 1949a; DeLange, 1950). The increase in weight is due to enlargement of the cortex, primarily from cellular hypertrophy of the zona fasciculata. Garm reported that "the zona glomerulosa usually seemed to be wider in the nymphomaniac cows than in the endocrinologically normal cows." However, he was not able to obtain accurate measurements of the different zones of the cortex. He also stated that "The amount of cortical nodules seemed to be somewhat larger in nymphomaniac cows than in normal cases, but the variations were too large to permit definite conclusion in this respect."

Nodules of hyperplastic cortical cells are a prominent feature of the zona fasciculata in bulls over 3 to 4 years of age. Therefore, the development of hyperplastic nodules in the adrenal cortex of cows with cystic follicles may be one of the lesions associated with masculinization. So-called "adrenal virilism" in cattle has been overemphasized. If primary adrenal virilism does exist in the cow it must be exceedingly rare. Garm (1949b) discussed "adrenal virilism" and reported that "The ovaries are quite small and sclerotic, or cystically degenerated (these are sometimes lutein cysts)." The gross and microscopic changes in the "small and sclerotic" ovaries were not described so it is not possible for the reader to determine whether small cysts, which could have caused the clinical manifestations, were present or not. As far as I can determine, true cases of adrenal virilism do not occur in the cow and those that have been reported are merely cases of chronic cystic follicular degeneration that develop masculinization. Jubb and Kennedy (1970) stated that "It is misleading, and emphasis misplaced, to classify any ascertainable manifestations of oestrogen-induced adrenal heterofunction as a separate syndrome of adrenal virilism; they are merely at one end of a spectrum of structural and behavioral responses to functional cystic ovaries, the whole of which can be duplicated by the direct and indirect actions of parenterally administered oestrogens." Short (1962) concluded that it is "doubtful if adrenal virilism really exists in cattle."

The etiology of cystic follicular degeneration in cows has been reviewed by Garm (1949a), DeLange (1950), Dawson (1957), and Roberts (1971). Cystic follicular degeneration is a disease principally of European breeds of dairy cattle, but it may also affect beef and zebu cattle if they are withheld from breeding for prolonged periods of time. The failure to establish pregnancy, for a variety of reasons, predisposes cattle to the development of follicular cysts. This appears to be one of the reasons why many early researchers reported an apparent relationship between uterine infections and follicular cysts, the infections resulting in prolonged periods of infertility. In northern latitudes the disease occurs more frequently during the winter months when cows are closely confined in stables. Roberts (1971) suggested that "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." Garm (1949a,b), Eriksson (1954), Henricsson (1956), and Marion and Gier (1968) reported that follicular cysts occur more frequently in high-producing cows. However, it has been demonstrated in Sweden that the level of milk production can be increased while the incidence of follicular cysts is being reduced by selection of sires from families of cows that do not develop follicular cysts (I. Settergren, personal communication, 1979).

Eriksson (1954) demonstrated that inheritance plays a significant role in the etiology of follicular cysts in cattle. Henricsson (1956) assumed that the disease had a monogenic background and that the variation of manifestation in individuals is due to the combined effects of inheritance and environmental factors. In a study of the frequency of cystic follicular degeneration in cows of two Swedish A.I. Associations, he found that the risk for cystic ovaries increased from 0.3% in heifers to 8 to 10% in cows 4 to 5 years of age. About 50% of the cows living to 10 to 11 years had had cystic ovaries at least once during their life.

Follicular cysts in the cow have been induced experimentally with a variety of hormones. The injection of 5 mg of estradiol valerate, late in the estrous cycle (15th and 16th day), induced follicular cysts in 7 out of 10 heifers (Wiltbank, 1966). Follicular cysts developed in 7 out of 9 cows when adrenocorticotropin was administered daily during the follicular phase of the estrous cycle (Liptrap and McNally, 1976). Nadaraja and Hansel (1976) produced follicular cysts by injecting 5 mg estradiol valerate intramuscularly on Day 16 of the estrous cycle in cows and by injecting 100 ml of antiserum to bovine LH before the onset of estrus. The estradiol-induced cysts were thin-walled and 2.5 to 3 cm in diameter, whereas the LH antiserum-induced cysts were 5.0 to 6.0 cm in diameter and firm. They concluded that "cystic ovaries could result from premature LH release or an insufficiency of LH at the time of ovulation." Fathalla *et al.* (1978) reported that "Injection of increasing doses of testosterone during the follicular phase of the oestrous cycle resulted in the cystic ovarian condition in experimental cows." Ovarian follicular cysts, which are experimentally produced by a variety of methods, undergo spontaneous regression in the presence of a normal uterus. The cysts persist when the endometrium is damaged by intrauterine injections of Lugols' iodine solution or a culture of *Escherichia coli* organisms (Fathalla *et al.* 1978).

Sow. Cystic follicular degeneration is an important cause of infertility in swine. Nalbandov (1952) classified cystic follicles into two groups based on cyst size. Multiple large cysts that measured up to 5 cm in diameter and frequently contained patches of luteal tissue in the wall were found most frequently. These cysts contained small amounts of estrogen and large amounts of progesterone. Small, multiple cysts that measured 1 to 1.5 cm in diameter with little or no luteinization of the cyst wall were seen only occasionally. These cysts had high concentrations of estrogen and small amounts of progesterone.

Miller (1984) reported that "Cystic ovaries account for approximately 10% of the reproductive problems in swine sent to slaughter for infertility. Ovarian cysts can cause low conception rates, erratic estrous cycles and aggressive behavior. Nymphomania, which has been observed in cattle with cystic ovaries, has not been described in swine. Swine with ovarian cysts may be intermittently or permanently in anestrus, thus leading owners to a misdiagnosis of pregnancy."

Single cysts, which can be quite large, appear to have little if any effect on reproduction in the sow. Perry and Pomeroy (1956) reported that "No pregnant animal was found with ovaries containing more than one cyst of 15 mm in diameter or more." They concluded that "the maintenance of pregnancy appears to be impossible when the ovaries contain more than one cyst of about 15 mm diameter, or any very large cysts or a cluster of smaller ones, or one cyst and a number of cystic corpora lutea."

Casida (1934) reported that "when ovulation was produced by luteinizing hormone preparations following treatment with a follicle-stimulating extract, it occurred in the smaller (8 to 10 mm) follicles and not in the larger (11 to 15 mm). It seems very likely that these larger follicles had become somewhat cystic and would not react as readily as those of normal size."

Multiple cystic follicles have been induced in sows by injection of adrenocorticotrophic hormone during the follicular phase of the estrous cycle (Close and Liptrap, 1975). Large, multiple cystic follicles were induced in three sows and small multiple cystic follicles in three other sows. The plasma progesterone levels were relatively high in sows with large follicular cysts and low in those with small cysts. It appeared that the level of progesterone production was related to the degree of luteinization of the cysts. It was proposed that small cysts develop when the follicles are affected during the early stages of follicular growth and large cysts develop when follicles are more fully developed.

The administration of progesterone can also induce cystic follicles in the sow (Ulberg *et al.*, 1951; Baker *et al.*, 1954). Close and Liptrap (1975) stated that "Since corticosteroids do not appear to induce the cystic follicular condition in the sow, the possibility exists that progesterone of adrenal origin may serve, at least in part, as a component in the aetiology of this condition of infertility."

Naturally occurring cystic follicles in swine usually persist, but the experimentally induced condition regresses if the uterus is normal. Liptrap and McNally (1977) studied the effect of the uterus on induced cystic ovarian follicles in the sow. Complete bilateral hysterectomy resulted in persistence of large follicular cysts until euthanasia at 35 to 51 days following surgery. Atresia of large cysts occurred 15 to 18 days following a sham–hysterectomy experiment. Unilateral hysterectomy resulted in persistence of large cysts on the ovary on the side from which the uterine horn was removed and atresia of cysts in the contralateral ovary.

Bitch. Follicular cysts do not occur as frequently in the bitch as other types of pathologic ovarian cysts. The frequency of occurrence of follicular cysts in the bitch has been overestimated because other types of cysts have been mistaken for follicular cysts. Andersen and Simpson (1973) reported that follicular cysts were not the prevalent type in an aging Beagle colony. Follicular cysts were found in 3% of the dogs. In contrast, Dow (1960) reported that follicular cysts were the most common type of nonneoplastic cyst in the canine ovary with an incidence of 16%. My observations support the findings of Andersen and Simpson (1973).

Follicular cysts in the bitch can be associated with various signs of hyperestrogenism, including prolonged estrous periods, attraction of male dogs, edema of the vulva, and vulvar discharge. Many, however, do not exhibit specific manifestations of ovarian malfunction. Dow reported no histologic evidence of estrogenic activity in any of his cases of follicular cysts. According to Andersen and Simpson (1973), "the presence of follicular cysts could not be correlated with endometrial changes since some of the dogs were in anestrus and the others were in varying stages of metestrus."

Cystic follicular degeneration in the bitch differs from that in other species of domestic mammals in that granulosa cells tend to persist in the wall of cystic follicles. In the cow and sow most or all the granulosa cells degenerate in long-standing cysts. In some bitches, especially those manifesting signs of hyperestrogenism, proliferating cords of elongated cells with clear cytoplasm line the cysts and extend into the adjacent connective tissue. Approximately 50% of the cases in the bitch have patches of lutein tissue lining the cysts.

The extraovarian lesions associated with follicular cysts in the bitch have not been studied very thoroughly. Andersen and Simpson and Dow did not find significant uterine lesions. However, cystic hyperplasia of the progestational type leading to pyometra and cystic hyperplasia of the estrogenic type has been seen in cases of follicular cysts in the bitch. Those with progestational hyperplasia of the uterus have had cysts with areas of luteinization and those with estrogenic hyperplasia have had proliferating granulosa cells lining the cysts.

Queen. Relatively little is known about follicular cysts in the cat. A variety of other types of ovarian cysts have been mistaken for follicular cysts. Cats with follicular cysts may manifest signs of hyperestrogenism. Some may show signs of estrus at frequent intervals while others are in constant estrus for prolonged periods of time.

Ewe and Doe (Goat). Edey *et al.* (1977) reported that failure to ovulate at their first estrus ranged from 6.6 to 33% in three groups of puberal sheep. They stated that the "Duration of estrus and intensity of overt estrus symptoms in these animals were the same as in their ovulating contemporaries. . . . In some animals, failure of ovulation was followed by luteinization of a large follicle."

Grant (1934) reported that the most common size of mature follicles in the ewe was 9 to 10 mm, while a few 15- to 18-mm follicles were found. "The occurrence of particularly large follicles is probably due to definitely delayed rupture, for in several instances, they were found co-existent with corpora lutea two to three days old. Apparently, these follicles sometimes fail to rupture and develop into cysts. These may be 15 to 25 mm in diameter; each is surrounded by a fibrous capsule up to 3 mm in thickness" (Grant, 1934). Only six cases of follicular cysts were found in approximately 4000 ewes, and they did not interfere with the estrous cycle. Gustafsson and Holmberg (1966) reported a 0.6% incidence of ovarian cysts in sheep in a slaughterhouse survey of 502 organs.

Lyngset (1968) examined the reproductive organs from 1020 slaughtered goats and reported that 24 (2.4%) had ovarian cysts. Most of the cysts were unilateral and single with the size varying between 1.2 and 3.7 cm.

Mare. Follicular cystic degeneration, comparable to the condition occurring in other species of domestic mammals, does not occur in the mare. The condition has been diagnosed frequently on clinical examination, but gross and histologic examination of the gonads fails to substantiate the clinical diagnosis. Some mares manifest long periods of estrus early in the breeding season but the estrus cycles become normal as the season progresses. Ginther (1979) reported that "Mares are very dependable ovulators once the transitional period between anovulatory and ovulatory seasons is completed; that is, after the first ovulation of the year has occurred."

Two types of mares have been suspected of having follicular cysts. The first type is the mare that is normal except when in estrus. These mares are unusually intractable during estrus and return to normal behavior after estrus or ovariectomy. The second type is described as nymphomaniacal. Arthur (1963) reported that this "syndrome occurs irrespective of the phase of reproductive activity and continues without abatement into the period of winter anestrus, the nervous derangement has apparently become fixed and independent of female hormone; ovariectomy cannot then be expected to effect a cure."

Kenney and Ganjam (1975) reported that "A 10-cm cystic structure which occupied and virtually obliterated the left ovary was found in a four-month-old Quarterhorse filly which had died of other causes." Portions of the cyst wall were lined by granulosa cells, and "Other areas of the cyst wall were similar to a follicle in advanced atresia." The cyst fluid contained 1700 pg/ml of total estrogens.

Bowen (1968) reported on the induction of a cystic ovarian condition in the mare by feeding a progestogen-melengesterol acetate (MGA). Bowen stated that "The cystic follicles remained for a considerable time, and during the period of anestrous right round until the next breeding season, suggesting that the ovaries remained in this same condition all through the winter until a new cycle was triggered off in the spring."

Luteinized Follicles

A luteinized follicle (luteal cyst, luteinized cyst) develops where there is an apparent faulty release of luteinizing hormone (LH) resulting in ovulation failure but with sufficient LH to induce a complete lining of luteal cells in the anovulatory follicle. The diagnosis is based on the presence of a large spherical cyst lined by a complete rim of luteal tissue and the absence of an ovulatory protrusion on the surface of the ovary. This appears to be a relatively uncommon condition in cattle as judged by the examination of slaughterhouse specimens.

The use of luteinizing hormone to induce superovulation in the cow commonly induces luteinization without ovulation. Archbald *et al.* (1973) studied the sequential morphologic changes in the ovaries of heifers that had been treated with gondadotropins. They stated that "The unruptured, luteinized follicles in ovaries from heifers treated with exogenous gonadotropins were microscopically similar to spontaneous follicular and luteal cysts of cystic ovarian degeneration in the cow."

Ginther (1979) reported a form of apparent ovulatory failure in the mare. He stated that "The preovulatory follicle grows to an unusually large size (e.g., 70 to 80 mm), fails to ovulate but fills in with blood and then gradually recedes. The unruptured hemorrhagic follicle may develop a complete or partial thin wall of luteal tissue or may remain devoid of grossly visible luteal tissue." These cysts occur during the autumn and are probably what others have called "autumn follicles."

Individual luteinized follicles occur occasionally in apparently normal bitches and sows. These minor ovarian defects are apparently due to a retarded maturation of the affected follicles at the time of luteinizing hormone release.

Friedgood and Foster (1938) reported the occurrence of 5- to 7-mm luteinized follicles in adrenalectomized cats that had been treated with follicle-stimulating and luteinizing hormones. They concluded that "The development of extraordinary lutein cysts seems to be definitely associated with the absence of the adrenal glands. These huge lutein cysts were observed in the ovaries of cats showing adrenal insufficiency, as well as those adequately supported by cortin. It would appear, therefore, that a substance other than the life-sustaining hormone of the adrenal cortex is involved in their pathogenesis.

Cystic Corpora Lutea

A cystic corpus luteum develops following ovulation and appears to be due to premature closing of the rupture site with the formation of a cyst in the center of the developing corpus luteum. An ovulation papilla or bulge is present (Fig. 4.1), and this differentiates a cystic corpus luteum from a luteinized cyst. A cystic corpus luteum has a zone of fibrous tissue between the luteal cells and the cystic cavity (Fig. 4.2).

Cystic corpora lutea can be diagnosed most readily in the cow when the corpus luteum reaches its maximum size at midcycle. The overall diameter of a cystic corpus luteum is usually larger than a normal corpus luteum and an ovulation bulge is present. The mass of luteal tissue is usually more spherical than a normal corpus luteum but not as round as a luteinized cyst. In a study of 357 postpartum cycles in cows, Morrow *et al.* (1966) found that cystic corpora lutea were present in approximately 25% of the cycles. No adverse effects of the cystic corpora lutea on reproductive function were detected. Therefore, it appears that cystic corpora lutea occur frequently in cattle, and generally with sufficient progesterone production to initiate and maintain pregnancy. Some cystic corpora lutea may produce inadequate levels of progesterone but the same may be said for solid corpora lutea. Cystic corpora lutea are seldom found in European breeds of cattle that have passed 40 to 50 days of gestation because previously existing cysts usually become obliterated by connective tissue by this time.

Cystic corpora lutea of pregnancy occur in zebu cattle (Resende *et al.*, 1972). The ovaries of zebu cattle

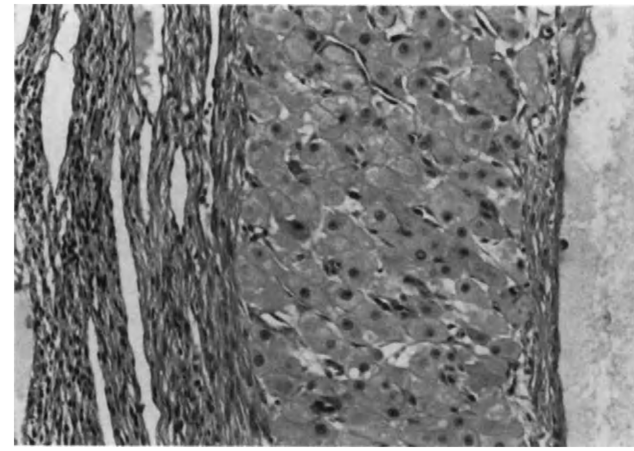

Fig. 4.2. Feline cystic corpus luteum. ×178. Acc. No. 18641.

are significantly smaller than those of European cattle. Corpora lutea frequently bulge considerably above the surface of the ovary and it is not unusual for most of the luteal tissue to be located above the ovarian surface. Consequently when a cyst occurs in a corpus luteum of a pregnant zebu cow, it bulges above the surface of the corpus luteum and continues to enlarge during pregnancy. The cyst may be several times larger than the ovary (Fig. 4.3) in advanced pregnancy. The involution of the corpus luteum during the postpartum period results in a loss of fluid in the cyst. The cyst becomes pedunculated, undergoes torsion, and drops into the peritoneal cavity, leaving only a small scar on the surface of the ovary.

Cystic corpora lutea occur occasionally in other species of domestic mammals; as in cattle, they do not appear to be of clinical significance. There is no apparent relationship between cystic corpora lutea and cystic follicles or luteinized follicles.

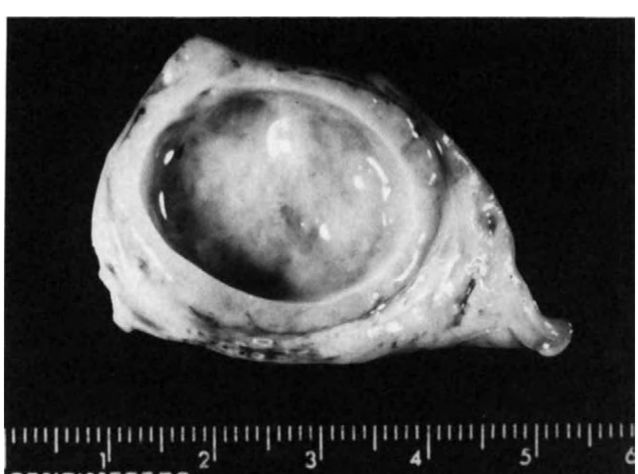

Fig. 4.1. Incised bovine ovary containing a cystic corpus luteum. The luteal tissue bulges above the ovarian surface, indicating that ovulation has occurred. Acc. No. 18016.

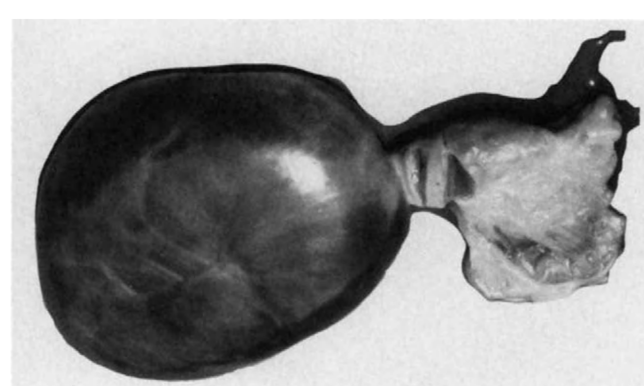

Fig. 4.3. Cystic corpus luteum from a zebu cow. The corpus leteum was incised and some cyst fluid escaped from the ovary. Acc. No. 13309. (Photo provided by Dr. Francisco Megale, Belo Horizonte, Brazil.)

Epithelial Inclusion Cysts

Inclusion cysts of the surface epithelium of the ovary are frequently referred to as "germinal inclusion cysts." This is a misnomer because the surface epithelium is modified peritoneum and not germinal epithelium. Surface epithelium becomes pinched off from the surface of the ovary and embedded in the peripheral part of the ovarian cortex following ovulation. Manual trauma to the ovary caused by enucleation of corpora lutea or rupture of follicular cysts may induce the formation of inclusion cysts of the surface epithelium in cattle. In domestic mammals, except the mare, the cysts are usually small, rarely exceeding a few millimeters in diameter, are located near the surface of the ovary, and are of no clinical significance. The cysts are lined by a single layer of cuboidal to flattened epithelial cells and contain clear watery fluid.

In the mare, inclusion cysts of the surface epithelium originate in proximity to the ovulation fossa and have been called "fossa cysts" (Prickett, 1966; O'Shea, 1968). The cysts are multiple, increase in number and size with age, and gradually destroy much of the parenchyma of the ovary (Figs. 4.4 and 4.5). A large number of cysts can block ovulation and in advanced cases most of the gonad is destroyed, resulting in a nonfunctional ovary.

R. B. Hillman (personal communication, 1970) has breeding records on a 17-year-old Thoroughbred mare in which three large cysts were known to be present in the left ovary for a period of 3 years. During this time, the right ovary functioned normally and the mare became pregnant two times during the 3-year period. Ovulation did not occur from the left ovary during this time. The affected ovary, which was surgically removed, contained three epithelial inclusion cysts up to 4.5 cm in diameter and multiple, small cysts below the ovulatory fossa. Most of the normal ovarian tissue was destroyed.

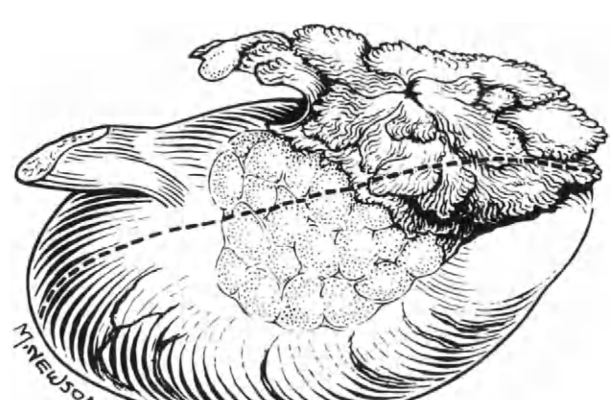

Fig. 4.4. Equine ovary with epithelial inclusion cysts protruding into the ovulation fossa. The broken line indicates the plane of section for Fig. 4.5. Acc. No. 8654.

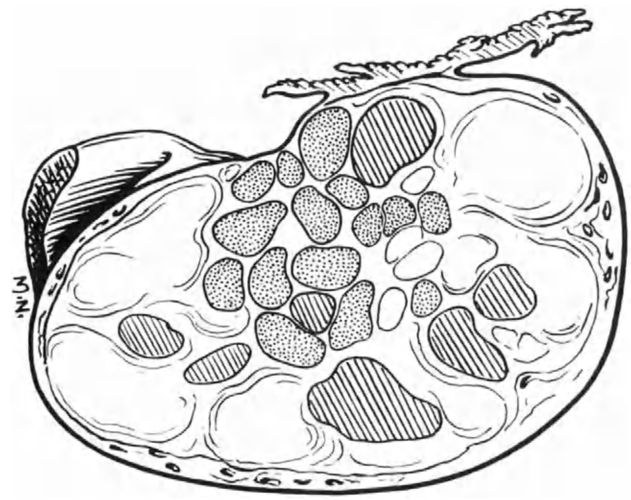

Fig. 4.5. Longitudinal section of equine ovary. Stippled areas are epithelial inclusion cysts, and striped areas are follicles. Acc. No. 8654.

O'Shea (1968) described the histology of inclusion cysts ("fossa cysts") of the surface epithelium in the equine ovary. A large portion of the ovulation fossa, adjacent to the infundibulum of the uterine tube, is covered by columnar epithelial cells, many of which are ciliated. These pseudostratified ciliated columnar cells are an extension of the epithelium of the uterine tube. The epithelium in the rest of the ovulation fossa is cuboidal or squamous, like that covering the ovary in other species of domestic mammals. The transition from the columnar to cuboidal epithelium is abrupt. The epithelial inclusion cysts in the mare originate from two types of epithelium: the tubal (paramesonephric) epithelium and the peritoneum. Thus, the inclusion cysts in the mare differ from those in other species of domestic mammals not only in their ability to cause fertility problems but also in the morphology of the epithelial lining.

Cysts of the Subsurface Epithelial Structures

O'Shea (1966) proposed the term subsurface epithelial structures (SES) for the tubules and cords of cells located beneath the surface epithelium of the canine ovary. These structures are not present in the postnatal ovaries of other domestic mammals. The SES are an ingrowth of the peritoneal covering of the ovary and they continue to develop throughout life. They are lined by a single layer of cuboidal cells and can be distinguished from the underlying granulosa cell islands because the latter are lined by several layers of columnar cells.

O'Shea found that intracytoplasmic acid mucin droplets containing sialic acid were present in the SES cells but absent in other epithelial structures in the canine ovary. The droplets were demonstrated with the alcian blue/PAS and colloidal iron stains for acid mucins. O'Shea stated that the droplets "were rounded or irregular in shape, and often formed large and conspicuous clusters in which individual droplets were variably fused. Individual droplets were usually less than 4 μ in diameter, and were smaller than the cell nuclei." The droplets were only rarely detectable as faintly stained droplets in hematoxylin eosin and periodic acid Schiff stained sections. The SES were not found to be directly related to primary follicles and acid mucin droplets were not found in the cytoplasm of granulosa cells as they were in SES cells.

Cystic SES are not seen in young bitches but they occur with increasing frequency with advancing age. It is a much more common cystic condition of the canine ovary than cystic follicular degeneration. Cysts of the SES are sometimes confused with those of the epoöphoron. Cysts of the SES are seldom larger than 5 mm and are located throughout the ovarian surface, whereas epoöphoron cysts may be as large as 4 to 5 cm and are located near the ovarian hilus. It is not unusual for both types of cysts to occur in the same ovary, especially in aged bitches.

SES cysts are lined by a single layer of cuboidal epithelial cells (Figs. 4.6 and 4.7) in contrast to cystic follicles, which may be lined by several layers of granulosa cells, fibrous tissue, or patches of lutein cells. Numerous SES cysts may be present in the ovary without apparent effect on ovarian function. Corpora lutea in various stages of development and regression are found frequently in association with SES cysts.

Cystic Rete Ovarii

Cystic rete tubules occur in all species of domestic mammals but are most common in the dog and cat.

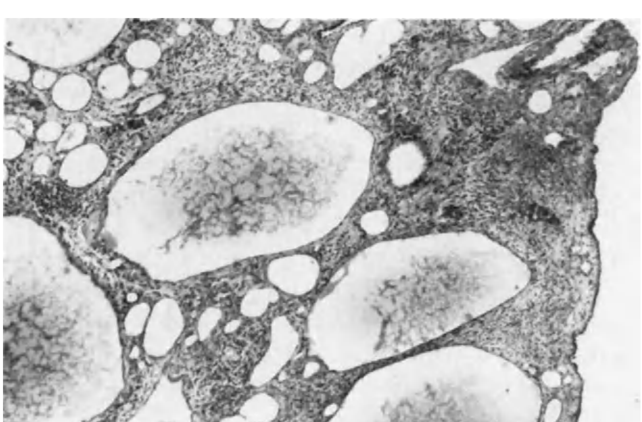

Fig. 4.6. SES cysts in canine ovary. There is considerable variation in the size of the cysts. ×56. Acc. No. 9040.

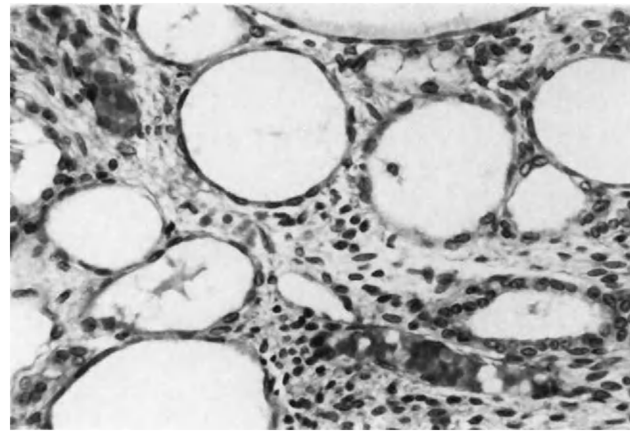

Fig. 4.7. SES cysts lined by a single layer of epithelial cells. ×222. Acc. No. 9040.

The lining of the anastomosing rete tubules consists of a single layer of epithelial cells. No smooth muscle surrounds the rete tubules in contrast to the mesonephric tubules, which are surrounded by a thin layer of smooth muscle fibers. This anatomical difference can be useful in differentiating epoöphoron cysts from rete cysts. The rete tubules sometimes communicate with the mesonephric tubules and cyst formation may involve both structures. The rete cysts have areas of papillary infolding of the wall as a result of marked distention of the lumina of anastomosing tubules. Cysts of the mesonephric tubules (epoöphoron) are usually oval or round without infolding of the wall.

Andersen and Simpson (1973) reported that "The rete ovarii in 10% of Beagles over eight years of age contained cysts of variable size; in another 5% the structure was greatly enlarged." In advanced cases the cysts virtually destroy the entire ovary.

Cysts of the rete ovarii in domestic mammals have been described most thoroughly in the cat (Gelberg *et al.*, 1984). In contrast to other domestic mammals, the cat may develop cystic distention of the rete ovarii at an early age. It has not been determined how early the process begins, but advanced lesions have been seen in cats as young as 7 months of age. One or both ovaries may be affected. The cysts are usually single and are 1 to 2 1/2 cm in diameter. They often cause severe compression of the ovarian cortex (Fig. 4.8).

The rete ovarii consists of three parts: an intraovarian rete, a connecting rete, and an extraovarian rete. The intraovarian rete is located within the tubal extremity of the ovarian medulla and is lined by cuboidal epithelium. The connecting rete is located at the tubal extremity of the ovary and is lined by ciliated columnar epithelium. The extraovarian rete consists of tubules lined by ciliated columnar cells, which end blindly in the periovarian tissue.

Fig. 4.8. Subgross micrograph of ovarian rete cyst and uterine tube from a 4-year-old cat. ×3.3. Acc. No. 16245. (Feline cystic rete ovarii. Gelberg *et al.*, 1984.)

Single Large Cyst

Granulosa cell neoplasms with a single large central cyst are discussed in conjunction with other types of ovarian cysts because they are occasionally confused with follicular cysts. In some cases the origin of the cyst fluid is difficult to establish because of necrosis involving much or all the lining neoplastic granulosa cells. It is a comparatively rare lesion that has been observed mainly in the mare, but a few cases have been found in the cow and bitch.

My attention was drawn to this condition by a report of Teige (1953) concerning a mare with an ovarian cyst. The fertility of the mare was normal, and she died because of incarceration of an intestinal loop. The mare was pregnant at the time of death. One ovary measured 13 × 11 × 8 cm with a large central cyst containing approximately 200 ml of thin, clear fluid. The cyst lacked an epithelial lining and the wall contained collagenous connective tissue.

Subsequently, I examined two similar cases that had been diagnosed as ovarian neoplasms on clinical examination. The first case was observed in a 10-year-old Arabian mare. An 8-cm cyst was detected early in the breeding season, and it became larger by the time the mare was bred. She conceived and delivered a normal foal. The affected ovary was surgically removed 4 months following foaling. The ovary weighed 206 g and consisted of a mottled fibrous mass. No prominent cysts were evident, but on histologic examination irregular masses of dense tissue resembling amyloid were evident. There were numerous accumulations of pigment-laden macrophages, indicating previous hemorrhage. Apparently the large cyst had ruptured during parturition.

The second case occurred in a 9-year-old Standardbred mare that had been infertile for 3 years. A greatly enlarged right ovary was removed surgically. The ovary was approximately 20 cm in diameter with a large central cyst containing about 500 ml of straw-colored, thin fluid. The cyst wall was coarsely granular and consisted of collagenous tissue that resembled amyloid but did not stain as amyloid.

In subsequent cases, the lining of the single large cysts was examined more thoroughly. It was discovered that some of the cysts had small areas of yellow to orange nodular tissue in the cyst wall. Histologic examination revealed foci of neoplastic granulosa cells. The major portion of the cyst wall was similar to that seen in previous cases. Thus, it appears that single large cysts with a predominantly fibrous tissue lining are cystic granulosa cell neoplasms in which the blood supply to the major part of the neoplasm has been obstructed as a result of the proliferation of collagenous tissue. It appears that they are self-destructing granulosa cell neoplasms.

Cysts around the Ovary

Cysts of Mesonephric Tubules and Ducts

The term "parovarian cyst" is commonly and incorrectly used to denote any type of cyst located around the ovary. It would be better to avoid the use of the term in favor of a specific designation for each type of cyst. The term parovarium refers to the epoöphoron (cranial mesonephric tubules). Cysts that arise from these structures should be called epoöphron cysts. Cysts in the vicinity of the ovary may also develop from vestiges of the caudal mesonephric tubules (paroöphoron), the mesonephric duct, and the blind accessory funnels, which are of paramesonephric origin.

There is very little literature on the histogenesis of cysts around the ovaries in domestic mammals. Gardner *et al.* (1948) reviewed the literature on broad ligament cysts in the human female and proposed a simple classification of the cysts. They stated that "The terminologic welter, histologic melange and embryologic diversities left us is a state of mind that could best be described as one of chaotic confusion." It does not appear that the terminology or understanding of cysts that occur around the ovary has improved very much during the last 40 years, especially as far as veterinary medicine is concerned. Gardner *et al.* classified cysts in the board ligament as mesonephric duct cysts, mesonephric tubule cysts, and paramesonephric cysts. They described the histology of the various types of cysts in a large series of normal and abnormal human specimens.

The mesonephric duct is lined by low cuboidal, nonciliated epithelium with mesially placed, moderately vesicular nuclei and surrounded by two layers of smooth muscle fibers. The mesonephric tubules are more highly convoluted than the mesonephric duct. They also have layers of muscle fibers but not as thick as in the mesonephric duct. The muscular coat is lost as the tubules approach the rete. The epithelial lining of the tubules consists of low columnar to cuboidal cells. Both ciliated and nonciliated cells are present. The ciliated cells have pale-staining cytoplasm and large, usually round, centrally placed nuclei. The cytoplasm of the nonciliated cells stains more darkly. Their nuclei are usually oval and centrally placed. The paramesonephric derivatives also have ciliated and nonciliated epithelial cells as well as a thin muscular coat. The nuclei of epithelial cells of paramesonephric origin are about 50% larger than those of mesonephric origin. Another criterion used for differentiating mesonephric and paramesonephric derivatives is the presence or absence of a basement membrane. Gardner *et al.* (1948) reported that "The mesonephric epithelium tubule has a well-defined basement membrane, as does its pathologic derivatives. The oviduct epithelium has no basement membrane."

Cysts of the epoöphoron (Figs. 4.9 and 4.10) occur in all species of domestic mammals and are located between the ovary and the fimbria of the uterine tube. The lining of the cysts consists of a single layer of cuboidal epithelial cells. Some of the cells are secretory and other are ciliated. A thin zone of smooth muscle surrounds the tubules. It is frequently difficult and often impossible to determine, on histologic examination, the origin of a cyst located around the ovary without knowledge of its location. Cysts of the

Fig. 4.9. Cystic epoöphoron in a bovine ovary. Acc. No. 8561.

Fig. 4.10. Cystic epoöphoron in a canine ovary. Acc. No. 17978.

epoöphoron are located on the tubal extremity of the ovary, cysts of the paroöphoron on the uterine extremity of the ovary, mesonephric duct cysts close to the uterine tube, and cystic accessory funnels are located on the serosal side of the fimbria of the uterine tube.

Although Gardner *et al.* (1948) found paramesonephric derivatives in locations where mesonephric tubules are usually found, I have not been able to identify paramesonephric derivatives in these areas in domestic mammals. Thus, I propose that the cysts of vestigial structures be classified according to their location until more definitive investigations have been conducted on these structures in domestic mammals.

Cysts of the epoöphoron may attain considerable size, especially in the mare and bitch. The cysts enlarge slowly over a long period of time so that large cysts occur predominantly in aged animals. In a report concerning reproductive function in mares, Arthur (1958) reported that "The largest cysts of the epoöphoron which on rectal palpation feels like a part of the ovary—were from 4 to 7 cm." They may be confused with large follicles on a single clinical examination. In the bitch, multiple epoöphoron cysts up to 1 cm in diameter and larger are present in the mesovarium and they extend into the ovary. Similar cysts are seen less frequently in the cat. In ruminants the cysts are usually small (1 to 3 mm) but may attain diameters of 1 to 3 cm. There is no definite evidence that the large cysts of the epoöphoron interfere with ovarian function.

Cysts of the paroöphoron rarely occur in domestic mammals. I have seen a few small (1 to 3 mm) cysts of the paroöphoron in the cow and the mare. These are located on the ovary adjacent to the proper ligament.

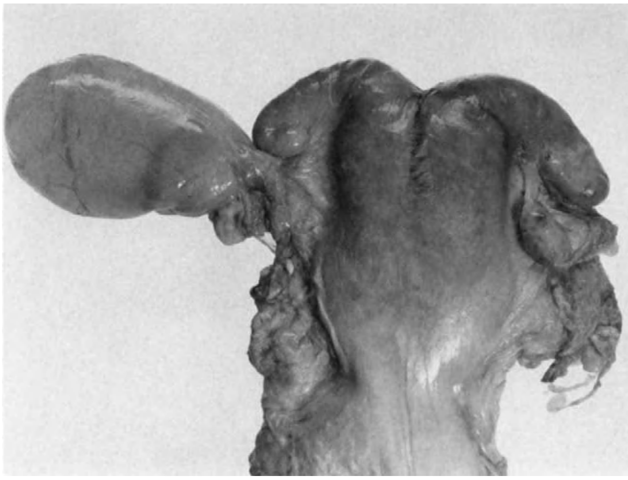

Fig. 4.11. Bovine tubo-ovarian cyst. Acc. No. 1211. (From Dobberstein *et al.*, 1985.)

Cystic Accessory Uterine Tubes and Accessory Funnels

Cystic accessory uterine tubes and cystic accessory funnels are discussed in Chapter 6.

Tubo-ovarian Cysts

The complete fusion of the fimbria of the uterine tube with the ovary in cases of salpingitis and perioöphoritis results in the accumulation of clear fluid in the proximal part of the uterine tube as the inflammation subsides. The resulting cystic distention of the uterine tube that is adherent to the ovary is known as a tubo-ovarian cyst (Fig. 4.11). It occurs in cattle as a comparatively rare condition (Gilman, 1921). It is seen more frequently in areas where brucellosis is widespread.

Cystic Ovarian Bursa

The cystic ovarian bursa develops when a portion of the fimbria of the uterine tube adheres to the ovary and fluid from the tube flows into the bursa causing distention of the bursa. This condition is seen predominantly in cows as a sequela to serve inflammatory diseases of the uterine tube and ovarian surface. Adhesions following enucleation of the corpus luteum in cattle may also result in cystic distention of the ovarian bursa.

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Chapter 5
Ovarian Neoplasms

Epithelial Tumors
- Papillary Adenoma
- Papillary Carcinoma
- Cystadenoma
- Cystadenocarcinoma
- Adenoacanthoma (Carcinoma with Squamous Metaplasia)
- Fibroadenoma
- Undifferentiated Carcinoma

Germ Cell Tumors
- Dysgerminoma
- Teratoma

Sex Cord–Stromal Tumors
- Granulosa Cell Tumor
- Thecoma (Theca Cell Tumor)
- Interstitial Cell Tumor (Luteoma, Lipid Cell Tumor)
- Androblastoma (Sertoli–Leydig Cell Tumor, Arrhenoblastoma)

Mesenchymal Tumors
- Hemangioma
- Leiomyoma
- Fibroma
- Lymphoma (Lymphosarcoma)

Secondary (Metastatic) Tumors

Tumorlike Lesions
- Adenomatous Hyperplasia of the Rete Ovarii
- Papillary Hyperplasia of Ovarian Serosa
- Stromal Hyperplasia and Hyperthecosis
- Vascular Hamartoma
- Ovarian Cysts

Bibliography

Ovarian tumors in animals have been reviewed by Parodi (1975) and Cotchin and Marchant (1977). They occur in all species of domestic mammals but appear to be most common in the bitch and the cow. Their actual incidence has not been determined because ovaries are not examined routinely in abattoirs nor at necropsy. When ovaries are examined during a necropsy, they are seldom examined histologically unless gross lesions are evident. Consequently, the majority of early neoplasms are overlooked. The study by Dow (1960) of ovarian abnormalities in the bitch provides an exception to the preceding statement. Sections were prepared from the ovaries of 400 unselected bitches that had been submitted for routine necropsy at the University of Glasgow Veterinary Hospital. Neoplasms were found in 93 bitches, and these animals had 127 tumors of various types in one or more sites. Twenty-five (27%) of the 93 bitches with neoplasms had primary ovarian tumors. Twenty percent of all neoplasms were ovarian in origin. The ovarian neoplasms were found only in bitches that were at least 5 years of age. An ovarian tumor was considered to be the primary cause of disease in only one case.

Cotchin (1959) provided data on the frequency of diagnosis of ovarian neoplasms in the dog based on surgical and postmortem material. Only 51 (1.2%) in his series of 4187 canine neoplasms were of ovarian origin. By comparing these results with those of Dow, it is apparent that the majority of ovarian tumors in the bitch are not diagnosed during routine necropsy. Although the majority of small ovarian tumors in the bitch appear to be unimportant clinically, the histologic examination of early tumors provides an insight into their histogenesis.

Hayes and Young (1978) conducted an epidemiologic study of canine ovarian neoplasms: "Histologically confirmed ovarian tumors were diagnosed in 94 dogs seen by 13 North American veterinary university hospitals and clinics from March 1964 through June 1976—epithelial tumors represented 60% of the case series and granulosa-theca cell tumors, 27%." Most of the epithelial tumors were probably of subsurface epithelial structure (SES) origin. The relative risk of occurrence of epithelial tumors increased with age, whereas the risk of occurrence of granulosa cell tumors had a generally constant risk through middle age. "Statistically significant risk was evident in the Pointer breed for epithelial ovarian tumors, and in the English Bulldog for granulosa-theca cell tumors" (Hayes and Young, 1978).

Since only 94 ovarian neoplasms were diagnosed in 13 veterinary colleges over a period of 12 years, it tends to confirm my earlier remark that many ovarian neoplasms in the bitch are probably overlooked. Each college diagnosed an average of 0.6 canine ovarian neoplasms per year.

The ovarian neoplasms that I have examined are from a collection assembled at the New York State Veterinary College over a period of 33 years. The collection includes 498 ovarian neoplasms from the following species: 276 canine, 139 bovine, 52 equine, 22 feline, 7 porcine, 1 caprine, and 1 ovine.

The World Health Organization (WHO) classification of ovarian neoplasms devised by Nielsen *et al.* (1976) is followed here, except for a few additions and modifications. The majority of ovarian neoplasms can be classified within three categories: sex cord–stromal tumors, epithelial tumors, and germ cell tumors. The WHO classification is modified as shown in the outline of this chapter.

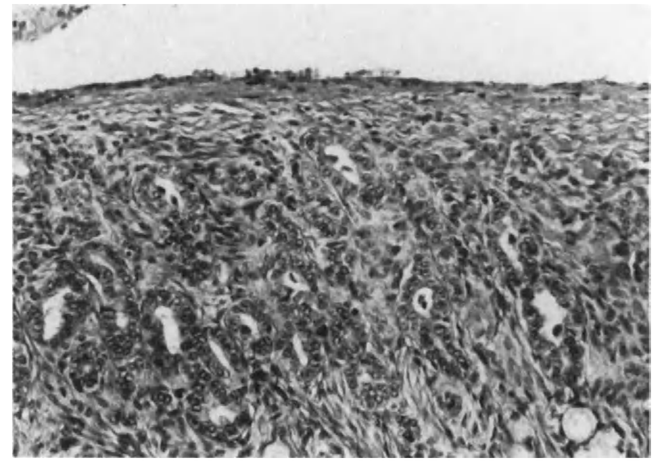

Fig. 5.1. SES adenoma in canine ovary. ×81. Acc. No. 11646.

Epithelial Tumors

Papillary Adenoma

Papillary adenomas of the ovary are rare in all domestic mammals except the dog. In the bitch they may arise from the surface epithelium, the subsurface epithelial structures (SES), or the rete ovarii. The majority of canine papillary adenomas develop from the SES and relatively few from the surface epithelium or rete ovarii.

SES Adenoma. Papillary adenomas (SES adenomas) that arise from the subsurface epithelial structures are frequently of multicentric origin and bilateral. They may have a smooth surface with nodular protrusions or a cauliflowerlike appearance due to compression of papillary projections by the mesosalpinx. The cut surface frequently contains cysts of varied size. The solid areas may be pink, gray-white, or pale yellow.

The early neoplasms appear as coarse infoldings and papillary projections of the epithelium into the lumina of the SES (Fig. 5.1). The papillae are covered by single or multiple layers of cuboidal to columnar epithelial cells that are pseudostratified in some areas. There is a mixture of ciliated and nonciliated cells with variable amounts of pale acidophilic, homogeneous cytoplasm. Some of the neoplastic cells consist predominantly of nuclei while others have abundant cytoplasm. The nuclei of the epithelial cells are usually oval and contain evenly dispersed, fine chromatin particles and small nucleoli, which are usually single. Mitotic figures are extremely rare in SES adenomas. The connective tissue cores of the papillary formations consist of loosely arranged, edematous fibrous tissue and blood vessels. The spaces around the papillary growths may be distended with proteinaceous material.

A variable quantity of cords and tubules are often present adjacent to the papillary areas of the neoplasm. The connective tissue stroma in these areas may consist of wide bands of intensely acidophilic tissue, occasionally containing roughly spherical laminated areas of mineralization. Some SES neoplasms start as compact tubular adenomas.

Papillary neoplasms of the canine ovary have been induced by prolonged administration of diethylstilbestrol (Jabara, 1959, 1962). Many of the experimentally induced neoplasms metastasized but then regressed following withdrawal of stilbestrol. The histogenesis of the experimentally induced tumors was studied by O'Shea and Jabara (1967). These tumors differed from spontaneously occurring SES neoplasms in several respects. The induced tumors arose predominantly from the surface epithelium of the ovary. Tubular structures were present beneath the proliferating surface epithelium. It was concluded that "These cell groups may have been formed directly from pre-existing SES, but it seems more likely that the majority arose from the surface epithelium in the same way that SES form in normal adult canine ovaries."

The SES extend into the cortex of the normal canine ovary only as far as the level of the primary follicles. In spontaneous SES neoplasms, the growths extend far into the ovary and out through the surface of the ovary. O'Shea and Jabara (1967) reported that the induced proliferative growths had "features suggesting hyperplasia rather then neoplasia. Thus, they were seen in a mild form after a short period (37 days) of stilboestrol administration, regressed following hormone withdrawal and never led to enlargement of the ovary beyond a diameter of 2 cm."

The histochemistry of SES adenomas and rete adenomas should be investigated to determine if histochemical differences in the epithelium of the two neoplasms exist. O'Shea (1966) found that the SES in the normal canine ovary secretes a sialic acid-containing mucin and that distinctive intracytoplasmic droplets of mucin are present in the SES but not in other epithelial structures in the canine ovary. O'Shea and Jabara (1967) found similar intracytoplasmic droplets of acid mucin in experimentally induced SES neoplasms in the bitch. The droplets were present in the primary neoplasm and in the metastases.

Rete Adenoma. Based on the lack of information in the literature, it appears that adenomas of the rete ovarii are rare. Nielsen *et al.* (1976) briefly mentioned adenomatous hyperplasia of the rete ovarii in the dog but the lesion was not illustrated. It is frequently difficult and sometimes impossible to differentiate between hyperplasia and neoplasia. Large proliferative lesions of the rete are considered to be neoplasms. It is quite likely that some of the reported papillary neoplasms of the canine ovary were of rete origin.

Rete adenomas can be identified primarily by their location in the tubal extremity of the ovarian medulla. The nonneoplastic portion of the rete is often cystic. The neoplasm consists of papillary projections of connective tissue covered by a single layer of cuboidal to columnar epithelial cells containing cilia (Figs. 5.2 and 5.3). The nuclei, which tend to pile up in some areas, are elongated and contain one to two small, centrally placed nucleoli. A few mitotic figures are usually present. The cytoplasm stains less intensely than that of SES neoplasms. The vascular connective tissue cores of the papillary projections are not edematous as they are in SES adenomas.

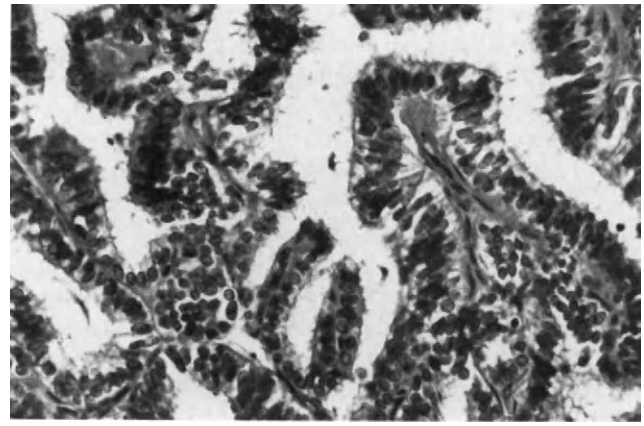

Fig. 5.3. Rete adenoma in canine ovary. ×222. Acc. No. 16193.

Papillary Carcinoma

SES Carcinoma. Most ovarian papillary carcinomas in the dog are of SES origin. The gross appearance is similar to that of the SES adenomas but they are usually much larger. The surface of the neoplasm may be smooth and nodular, cauliflower-like, or have a shaggy surface if it has extended through the ovarian bursa (Fig. 5.4). The opening to the ovarian bursa should be examined carefully in all cases of ovarian neoplasms in the dog. If the opening is widely dilated with protruding neoplastic tissue, the neoplasm is usually malignant. The SES carcinomas may have areas of necrosis and hemorrhage.

Metastasis occurs by implantation and by lymphatic and venous invasion. Tumor implants occur throughout the peritoneal cavity. Some are small, red, shaggy, soft masses and others are solid, firm, gray-pink nodules several centimeters in diameter.

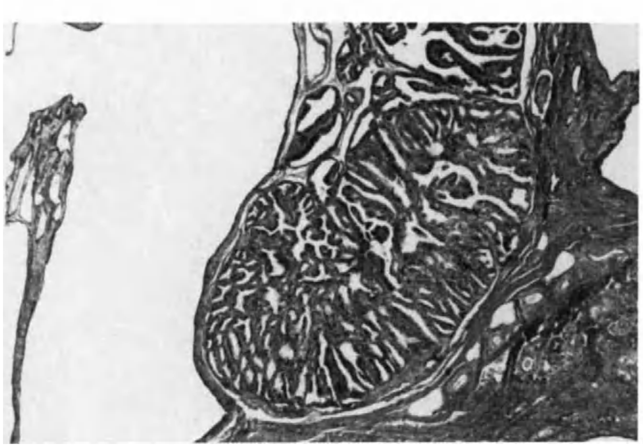

Fig. 5.2. Rete adenoma in canine ovary. ×22. Acc. No. 16193.

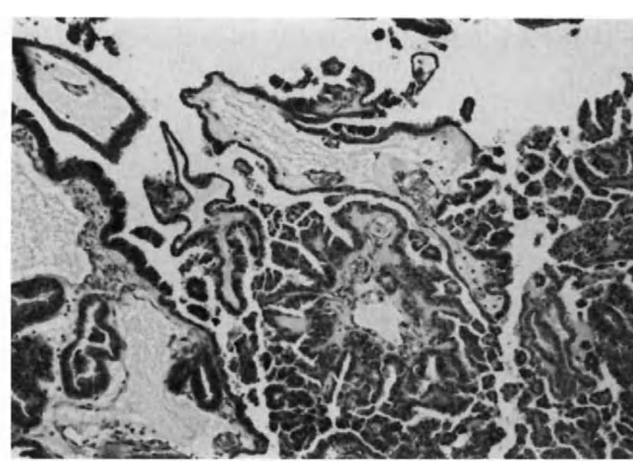

Fig. 5.4. SES carcinoma in a canine ovary. ×22. Acc. No. 19148.

The lymphatics in the diaphragm become occluded by neoplastic cells and cause ascites. The production of serous fluid by the neoplasm also contributes to the development of ascites. The ascitic fluid is frequently blood tinged. Metastases may be present in the bronchial lymph nodes, in lungs, and on the visceral and parietal pleura. In cases with pleural involvement, fluid accumulates in the thoracic cavity (Greene *et al.*, 1979). During clinical examination of aged, intact bitches with ascites, SES carcinomas should be considered among the possible differential diagnoses.

Relatively few data exist on the frequency of malignancy of SES neoplasms. Many of the neoplasms that are presented for histologic examination are surgical specimens from dogs on which long-term postsurgical information is not obtained. In a series of ovarian neoplasms in 69 bitches, Cotchin (1961) reported 20 adenomas and 5 adenocarcinomas. These neoplasms were probably of SES origin.

SES carcinomas with metastases beyond the ovary have mitotic figures that vary in frequency from scant to two to four per high-power field. The cells usually have less cytoplasm than in SES adenomas. Cells tend to pile up and form solid masses in some areas. Mitoses are more numerous in the solid areas and the nuclei are large and have one or two large nucleoli. Tumor thrombi are present in lymphatics and veins in the affected ovary.

Greene *et al.* (1979) reported an ovarian papillary cystadenocarcinoma in a 5 1/2-year-old Coonhound. The bitch had abdominal swelling of three months' duration that had begun just after the last estrus. Four liters of fluid were drained from the peritoneal cavity. Exploratory celiotomy revealed the presence of numerous tumor nodules on the serosa of all abdominal organs. Both ovaries were enlarged and contained fluid-filled cysts. The bitch was ovariohysterectomized and some of the nodules were removed for histologic examination. The bitch had hydrothorax as well as ascites. Anticancer therapy was administered, and the bitch was asymptomatic 10 months following surgery.

Rete Carcinoma. Carcinomas of the rete ovarii have not been reported in domestic mammals. Further studies are necessary to determine if some of the papillary carcinomas in animals are of rete origin.

Cystadenoma

Cystadenomas, which appear to arise from the epoöphoron and/or rete ovarii, are comparatively rare in domestic mammals. According to Nelson *et al.* (1967), Dobberstein found 10 cystadenomas in a series of 18 ovarian neoplasms in swine.

Ladds (1971) described a serous cystadenoma of the right ovary from a 13-year-old Pomeranian bitch. No clinical signs were associated with the presence of the tumor and the left ovary appeared to be normal. The neoplastic ovary contained a 2-cm cyst and several 2-mm cysts. The large cyst contained clear watery fluid. "A distinct nodule of solid tumor projected into the lumen of the major cyst and continued as fine strands across its lumen to attach to the opposite wall. . . . The cyst was lined mostly by squamous epithelium, although in some areas the lining cells were cuboidal or columnar. Numerous papillary projections were present in the lumen of the cyst, the remaining contents of which stained with eosin and PAS but not with alcian blue" (Ladds, 1971).

Dow (1960) recorded 8 serous cystadenomas in a series of 25 bitches with primary ovarian neoplasms. Many of these cystadenomas may have been of SES origin because "Intraluminal papillary growth was prominent in most specimens." Tanaka (1962) reported a canine cystadenoma "in which the rete ovarii showed a histological appearance similar to that of the tumor."

The cystadenomas that I have seen were serous and occurred predominantly in aged animals. One of 22 ovarian neoplasms in the cat and 14 of 276 in the dog were classified as cystadenomas. No cystadenomas were found in cows, sows, ewes, or does. Some of the tumors were bilateral (Fig. 5.5) and others unilateral. The largest canine cystadenoma measured 17 x 10 cm and weighed 572 g. The neoplasms consisted of multiple cysts up to 6 cm in diameter. The cysts were filled with clear serous fluid that did not coagulate upon fixation. The cysts were lined by a single layer of low cuboidal to flattened epithelial cells.

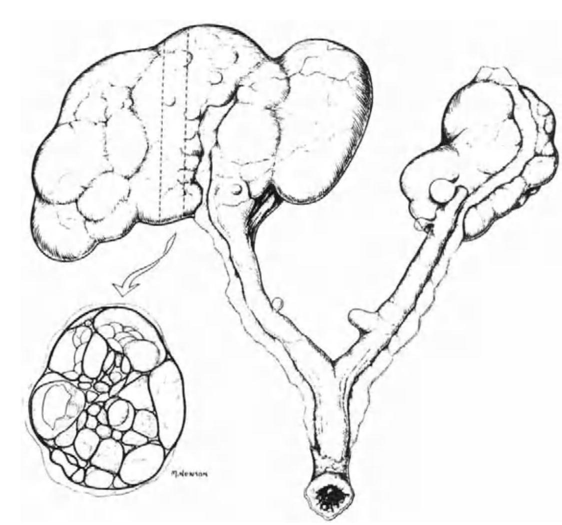

Fig. 5.5. Bilateral cystadenomas in canine ovaries. Serosal cysts and a leiomyoma on uterus. Acc. No. 5328. (From Dobberstein *et al.*, 1985.)

There was a small amount of dense fibrous tissue between the cysts. In advanced cases, the normal architecture of the ovary was destroyed completely, but in less advanced cases, a rim of compressed cortical tissue remained. It appears that many, if not all, of the cystadenomas, which lack papillary projections into the cysts, arise from the epoöphoron. Cysts of the epoöphoron are very common in aged bitches and it is often difficult to differentiate between large cysts of the mesonephric tubules and neoplasms. The cysts that result in marked enlargement of the ovary and cause destruction of most or all of it are considered to be neoplasms.

Hughes *et al.* (1980) recorded a serous cystadenoma from a 16-year-old mare that was examined at her first estrus after parturition. A large cystic mass (15 x 9 x 9 cm) was found in the left ovary. Although the mare's testosterone levels were elevated (52 pg/ml plasma), she continued to cycle at regular 21- to 22-day intervals with ovulation occurring in the right ovary. The mare was bred and conceived during the next breeding season. The enlarged left ovary was removed during early pregnancy. It weighed 832 g and contained numerous thin-walled cysts filled with clear, serous fluid. "These cysts were lined by a low cuboidal epithelium which rested on an inactive fibrous stroma. Mitotic figures were rare. The epithelium of the cysts strongly suggested its origin from the germinal epithelium of the ovulatory pit" (Hughes *et al.*, 1980). Another similar case was diagnosed clinically, but the affected ovary was not obtained for morphologic examination.

Held *et al.* (1982) reported an ovarian cystadenoma from a 13-year-old Thoroughbred mare. She had normal estrous cycles but failed to conceive during the year following her last foaling. A markedly enlarged right ovary was removed surgically and the mare died of hemorrhage following surgery. The affected ovary measured 26 x 20 x 15 cm, weighed 5 kg, and consisted of multiple large cysts containing clear, yellow fluid. The ovarian tissue weighed only 100 g after the cyst fluid was removed. Hormone analysis of the fluid "suggested that the tumor was a non-hormone producer." The cysts were lined by a single layer of cuboidal to flattened epithelial cells, many of which had apical cilia. The stroma consisted of dense collagenous connective tissue. The tumor was diagnosed as a serous cystadenoma and it was stated that "the adenoma probably originated from the surface epithelium of the ovulation fossa."

Cystadenocarcinoma

Sow. Anderson and Sandison (1969) reported two serous cystadenocarcinomas of the porcine ovary. The tumors had a "complex papillary pattern, with long slender fibro-vascular cores bearing one or sometimes several layers of epithelial cells which were of columnar type with wispy edges; some were vacuolated." They stated that the structure and appearance of the neoplastic cells were reminiscent of normal uterine tube. It is possible that these neoplasms may have originated in the rete ovarii. Metastatic lesions were found in the lung in one case.

Cow. Anderson and Sandison (1969) reported 3 papillary serous cystadenocarcinomas in a series of 11 bovine ovarian neoplasms. Metastases were present on the peritoneum, in the iliac nodes, and in the kidney.

Anderson and Sandison reported three mucinous cystadenocarcinomas of the bovine ovary. Peritoneal metastases were present in two cows and peritoneal, liver, lung, and pleural metastases in one cow. They stated that "these tumors showed a complex and irregular papillary formation of columnar cells arranged along vascular stromal areas. Mucoid areas were present where tumor cells streamed off into large mucin-filled spaces." Anderson kindly provided me with a paraffin block of tissue from one of the cases. The features of the neoplasm suggest that it was a malignant granulosa cell tumor with mucoid degeneration. When columnar-appearing cells were present, they were located adjacent to the connective tissue stroma and resembled the basal layer of granulosa cells that occur in mature follicles. Some of the cysts were lined by a single layer of cells and other cysts contained numerous layers of cells resembling granulosa cells. Some of the cysts contained mucoid material and pyknotic tumor cells. Loosely arranged mucoid-appearing connective tissue was present in a few areas. The neoplasm was not similar to the mucinous cystadenoma of women. Perhaps many, if not all, of the mucinous cystadenomas and cystadenocarcinomas that have been reported in domestic mammals were granulosa cell tumors with mucinous degeneration.

Morris *et al.* (1985) described an ovarian papillary adenocarcinoma in an 11-year-old Quarter Horse with ventral edema and dyspnea. The left ovary was about 15 cm in diameter and had a coarsely nodular surface. The thoracic cavity contained approximately 3 liters of dark red opaque fluid. Metastatic lesions were present in the sublumbar and tracheobronchial lymph nodes. A 35-cm neoplastic mass was located in the cranial mediastinum ventral to the trachea and attached to the medial surface of the left lung. The authors concluded that "The tumor could have originated from germinal epithelium, composed of mesothelial cells from the ovarian surface, or from paramesonephric (Müllerian) duct epithelial inclusions within the ovary. The latter possibility seems more likely, because the cystic structures within the ovary appeared as non-neoplastic paramesonephric inclusions."

Van Camp *et al.* (1989) reported an adenocarcinoma with teratomatous elements in the right ovary of a 9-year-old Appaloosa mare. She had regular estrous cycles and was bred once at 2 to 3 months after foaling. Seven months after breeding, the mare was found to be nonpregnant, and a 10- to 12-cm mass was palpated in the region of the right ovary. The mass was removed surgically, and the mare made an uncomplicated recovery.

"The excised mass measured 10 cm in diameter, with a predominantly smooth surface except for several raised nodular projections. Hemisectioning revealed a 7-cm-diameter eccentric cavity filled with approximately 250 ml. of red opaque fluid and solid, amorphous, gelatinous material that contained hair-like structures." Hair follicles were not found in sections and a definite diagnosis of "coexistent teratomatous elements" in the carcinoma could not be established. The neoplastic epithelial cells formed irregular ductular structures and solid sheets. "There was moderate pleomorphism of the cells, and the mitotic index was high. . . . In some sections, the bulk of the tumor was composed of densely packed mesenchymal cells forming whorls, interlacing bundles, and herringbone patterns. It was interpreted to be reactive stromal hyperplasia as has been described in women, but not in mares."

The condition of the mare deteriorated approximately 2 months after surgery, and she was killed. The abdominal cavity contained about 10 liters of serosanguinous fluid with masses of tan tissue up to 1 cm in diameter. Multiple tumors, similar to those found in the right ovary, were scattered throughout the abdominal cavity and in the lungs.

Adenoacanthoma (Carcinoma with Squamous Metaplasia)

Adenoacanthomas of the bovine ovary have been reported by O'Shea (1963) and Anderson and Sandison (1969); each reported single cases. The histologic features of the neoplasms consisted of acini with a single layer of columnar, cuboidal, or flattened epithelium. Other acini were more complex with simple or stratified epithelium that was often thrown into numerous papillary infoldings. Stratified squamous epithelium was present in some areas of the neoplasms, and the tumor reported by O'Shea had areas of keratinization.

Kay (1961) reviewed the literature concerning adenoacanthomas (ovarian carcinomas with squamous metaplasia) of the human ovary and reported four additional cases. He stated that the neoplasm "may be due to a metastasis from a uterine endometrial focus; or the growth may have arisen from ectopic endometrial tissue within the ovary. Finally, it may merely signify a metaplastic process following any type of adenocarcinoma arising within the ovary." The tumor in women occurs in relatively young patients (29 to 46 years of age) and "this represents a considerably lower age incidence than the usual ovarian or endometrial carcinoma." Patients with adenoacanthomas have a better prognosis than those with the usual ovarian carcinomas.

Fibroadenoma

The fibroadenoma is a rare ovarian neoplasm in domestic mammals. I have seen only one case in a series of 276 canine ovarian neoplasms. The tumor occurred in one ovary of a 7-year-old Cocker Spaniel bitch. It was confined in the ovarian bursa, presented a cauliflower-like appearance, and measured 13 x 5.7 x 10 cm with a weight of 432 g. The neoplasm was composed of abundant dense fibrous tissue containing cystic areas lined by single to multiple layers of cuboidal to columnar epithelial cells, many of which were ciliated. The fibrous tissue was arranged in coarse interwoven bundles.

Undifferentiated Carcinoma

It is not possible to identify the cell types in some very anaplastic epithelial neoplasms. These must consequently be classified as undifferentiated carcinomas.

Germ Cell Tumors

Not as many types of germ cell neoplasms of the ovary have been recognized in domestic mammals as in women. The main types in animals are dysgerminomas and teratomas. Dysgerminomas occur more frequently than teratomas in all species of domestic mammals with the exception of zebu cattle, in which benign cystic ovarian teratomas (dermoids) occur more frequently.

Dysgerminoma

The dysgerminoma is the counterpart of the testicular seminoma. Dysgerminomas have been reported most frequently in the bitch (McEntee and Zepp, 1953; Cotchin, 1961; Buergelt, 1968; Dehner *et al.*, 1970). They have been recorded in the cat (Dehner *et al.*, 1970; Andrews *et al.*, 1974), the sow (Lombard and Havet, 1962), the cow (Ball and Pommier, 1929; Chabasse, 1954; Summers *et al.*, 1975), the mare (McLennan and Kelly, 1977; Meuten and Rendano, 1978), and the goat (Smith, 1980).

Bitch. My series of 275 canine ovarian neoplasms includes 21 dysgerminomas. The majority of canine dysgerminomas occur in aged animals. The average age of Cotchin's (1961) series of 8 cases was 10.5 years. The 11 cases reported to Dehner *et al.* (1970) averaged 13 years of age. The youngest bitch in my series was a 2-year-old.

Clinical signs associated with the presence of dysgerminomas in the dog include abdominal enlargement with the presence of a palpable abdominal mass, bloody vaginal discharge, polyuria, emesis, weight loss, diarrhea, and lethargy. Cystic hyperplasia of the endometrium and cystic hyperplasia–pyometra complex occur in some cases and are probably responsible for some of the clinical signs.

Dysgerminomas in the bitch range in size from 2 to 30 cm, are spherical or ovoid, and have a smooth or coarsely lobulated surface. The cut surface is soft, rubbery, or firm, usually solid and white or gray (Fig. 5.6). Areas of necrosis and hemorrhage are present in many of the larger neoplasms. Ten to 20% of the cases are malignant. Metastases occur in the regional, mesenteric, and mediastinal lymph nodes, in various abdominal organs, in the omentum, on the serosa of the intestinal tract, and in the lungs.

The histologic appearance of dysgerminomas is quite similar in all species of domestic mammals. The neoplastic cells are arranged in sheets, cords, and alveoli. Cysts are present in a few cases. The tumor consists of a uniform population of polyhedral cells with light-staining amphophilic cytoplasm. The nuclei vary in size, are round, oval, or irregular in shape, contain abundant granular chromatin, and have one or two large nucleoli. Mitoses are numerous and sometimes abnormal. Multinucleated giant cells may be present. Diffusely scattered neoplastic cells undergo necrosis, leaving clear spaces that may contain macrophages with vacuolated cytoplasm (Fig. 5.7). The fibrous tissue stroma is usually scant; when abundant it may surround large masses of neoplastic cells or arrange these cells into cords. A lymphocytic reaction in the stroma, as occurs in testicular seminomas in all species and in human dysgerminomas, is comparatively rare in dysgerminomas of domestic mammals. The histologic appearance of benign and malignant dysgerminomas is similar.

I examined the reproductive organs from a 5-year-old Poodle bitch that was ovariohysterectomized because of dermatitis of suspected hormonal etiology. She had enlargement of the nipples, mammary glands, and vulva. One ovary contained a microscopic dysgerminoma. Germinal cells were proliferating in medullary tubules (Fig. 5.8) adjacent to the rete ova-

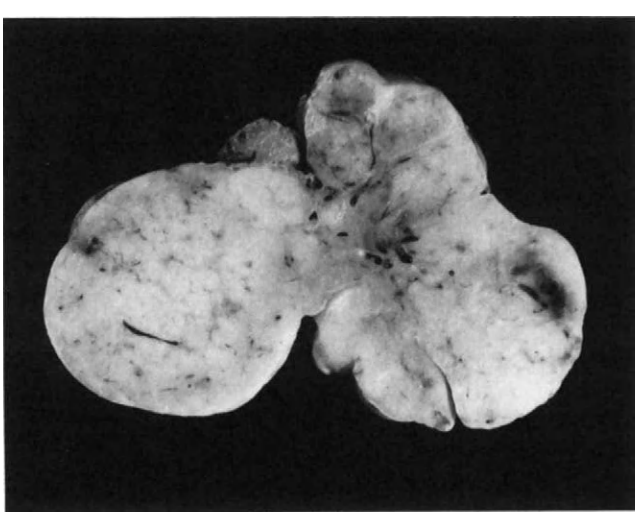

Fig. 5.6. Canine dysgerminoma; a gray, soft, 5.5 x 3.3 x 3.2-cm neoplasm. One-half of tumor extended out of ovarian bursa. Acc. No. 16570.

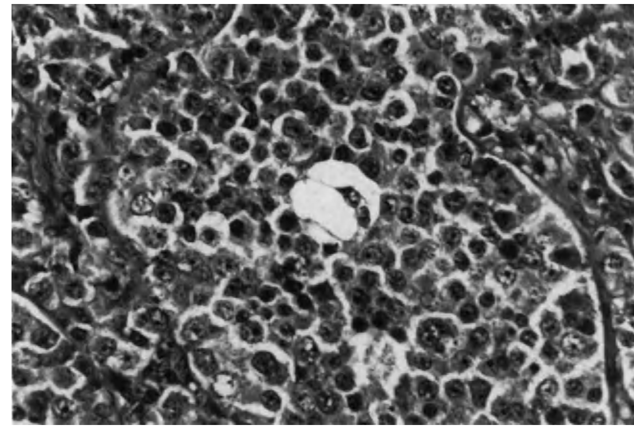

Fig. 5.7. Canine dysgerminoma. Macrophage with vacuolated cytoplasm in center of the photo. ×222. Acc. No. 16570.

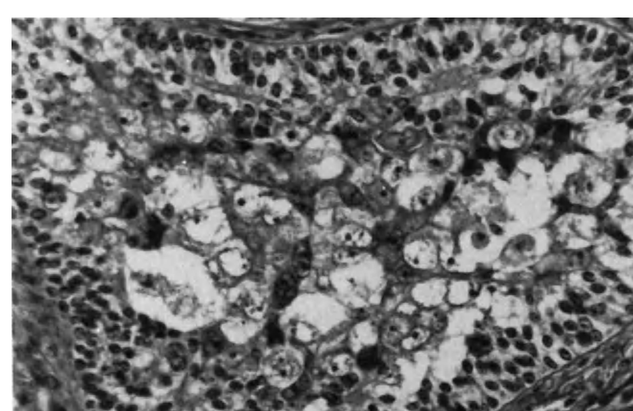

Fig. 5.8. Early formation of dysgerminoma in medullary tubule of a canine ovary. ×222. Acc. No. 11596.

rii. Some tubules contained only a few neoplastic germinal cells while others were distended with neoplastic cells. The neoplasm had not extended into the connective tissue adjacent to the affected tubules. In addition to the small intratubular dysgerminoma, the ovaries contained corpora lutea, atretic follicles, and SES cysts.

Queen. Dehner *et al.* (1970) reported a pure dysgerminoma in a 7-year-old Siamese cat and a mixed dysgerminoma and teratoma in a 6-year-old domestic cat. The Siamese cat exhibited masculine behavior. The affected ovary was 4 cm in diameter and the tumor had metastasized to the omentum. The mixed dysgerminoma–teratoma weighed 1000 g and no metastases were recorded.

There are six dysgerminomas in my series of 22 feline ovarian neoplasms. The ages of these affected cats were 1, 2, 5 (two animals), 7, and 18 years. Bilateral ovarian tumors were found in a clinically normal, 1-year-old domestic cat that was presented for routine ovariohysterectomy. The cat was in good health 2 years after surgery. This case was reported by Andrews *et al.* (1974). The 2-year-old cat had recurrent high fever and became emaciated following ovariohysterectomy to remove a diseased uterus and decomposed fetuses. The ovaries were not examined. Exploratory laparotomy at a later date revealed a moderate volume of clear, straw-colored fluid in the abdominal cavity and many granulomatous lesions on the serosa of the small intestine. Histologically these lesions were found to be metastases of a dysgerminoma. One 5-year-old cat had bilateral ovarian tumors each of which measured about 6 x 4 x 4 cm. No postsurgical information was available. The 7-year-old cat had anorexia, lethargy, weight loss, and anemia. A 9-cm dysgerminoma was present in the right ovary. The 17-year-old Siamese cat was in continual estrus and a mass was palpable in the abdominal cavity. The palpable mass was an ovarian dysgerminoma and metastases were found in the omentum.

Mare. Two cases of hypertrophic osteopathy have been reported in mares with dysgerminomas. McLennan and Kelly (1977) examined a 4-year-old crossbred mare that had had two bouts of colic about 12 months apart. The mare was presented for examination because of a reduced appetite and loss of condition. She had subcutaneous ventral edema extending from the mammary glands to the pectoral region. Firm, painless swellings were palpated in the pectoral region. The horse was stiff when walked or trotted. On per rectal examination, a large, firm, spherical mass was palpated in the left abdomen and a nodular enlargement was detected around the aorta caudal to the left kidney. The mare was killed. The left ovary had been replaced by a 40-cm dysgerminoma that was adherent to the abdominal wall. Metastases were present in the left renal lymph node, posterior vena cava, and the splenic, anterior mediastinal, and cervical lymph nodes. Gross lesions were not observed in the lungs but a few microscopic embolic metastases were present in pulmonary arterioles.

Meuten and Rendano (1978) reported a case of osteopathy associated with a dysgerminoma in an 8-year-old Arabian mare. The mare had intermittent colic, anorexia, and progressive weight loss for 6 months. According to the owner, swollen extremities were noticed for 4 to 5 months. The mare was in continual estrus for the last month. All extremities had bilaterally symmetrical, hard, nonpainful swellings that were most prominent at the joints. A large, firm mass was palpated in the right ovary. The tumor was removed surgically and the mare was killed 2 days later. The ovarian tumor weighed 8.7 kg, was 27 cm in diameter, and was mottled white, tan, and black. Numerous cysts up to 6 cm in diameter were found on cross section. The cysts contained dark brown to black aqueous or gelatinous fluid. Analysis of the cyst content revealed the presence of 67.3 pg/ml of estradiol 17B and 1.2 ng/ml of progesterone. Tumor nodules were disseminated throughout the mesentery, on the peritoneal surface of the diaphragm, and on the surface of the liver, spleen, and stomach. The ovarian mass consisted of large sheets of uniform cells separated into multiple lobules by thick bands of mature fibrous connective tissue. The cysts contained proteinaceous fluid, desquamated tumor cells, and necrotic debris. Lymphocytic foci were not found in the neoplasm. Although the ovarian mass was a dysgerminoma, the nodules that were scattered throughout the peritoneal cavity consisted of multiple islands of mucus-secreting glands surrounded by thick bands of scirrhous connective tissue. The origin of the peritoneal lesions was not established.

Cow. The bovine ovarian dysgerminoma reported by Summers *et al.* (1975) was a firm, spherical, red-gray, 15-cm mass. The cut surface had a mottled appearance with focal areas of necrosis and hemorrhage. Metastases were present in the liver, diaphragm, lungs, and mediastinal lymph nodes.

Hormone Production. The manifestations of constant estrus and the occurrence of cystic hyperplasia of the endometrium in some affected animals suggest that some dysgerminomas may be involved in hormone production. Lynn *et al.* (1967) presented "ultrastructural and biochemical evidence for possible estrogen secretion by a dysgerminoma in the absence of clinical signs of hyperestrogenism." Meuten and

Rendano (1978) found that an equine dysgerminoma "contained 67.3 pg/ml of estradiol and circulating blood estradiol determinations were approximately double that expected in a mare at estrus. This apparently accounted for the signs of estrus reported in the history." According to Dehner *et al.* (1970), "approximately 2% of human dysgerminomas secrete chorionic gonadotrophin."

Teratoma

Teratomas are neoplasms arising from at least two and generally from all three germinal layers. Tissue representing any organ, except ovary or testis, may be present. Cotchin and Marchant (1977) reviewed the literature on ovarian teratomas in laboratory and domestic animals. In domestic mammals, ovarian teratomas occur most frequently in the bitch and in the cow. Ovarian teratomas have been recorded in the mare (Fujimoto and Sakai, 1955; Abraham, 1968), sow (Marajew, 1934), and ewe (Brandly and Migaki, 1963). I have examined 31 ovarian teratomas with the following species distribution: 17 canine, 9 bovine, 3 feline, and 2 equine. All the bovine cases were dermoid cysts of which 7 were provided by Dr. Silney A. Costa and Dr. Francisco Megale of the School of Veterinary Medicine, Belo Horizonte, Brazil.

Bitch. Ovarian teratomas in dogs generally occur in animals younger than those with other types of ovarian neoplasms. In the 17 canine cases I examined, the ages of affected bitches varied from 1 to 17 years and most were under 5 years of age. All canine teratomas were unilateral and five were malignant.

A few of the cases of benign ovarian teratomas in dogs were found during routine ovariohysterectomy in animals that had not shown clinical signs. Dogs with large ovarian teratomas may exhibit a variety of clinical signs, including lethargy, constipation, anorexia, weight loss, distended abdomen, palpable abdominal mass, abdominal pain, elevated temperature, and hemoperitoneum. Sudden death, due to massive hemorrhage, may occur following rupture of the neoplasm.

Canine ovarian teratomas usually vary in size from 2 to 10 cm. Benesch (1935b) reported a 2.5-kg ovarian teratoma in an 18-month-old bitch, and Clayton (1975) reported a 3.4-kg teratoma in a 5-year-old bitch. Ovarian teratomas usually have a smooth or coarsely lobulated surface. The color and consistency of the cut section vary according to the tissue components of the neoplasm and the degree of necrosis and hemorrhage. Usually the tumors are a mixture of hard and soft areas and cysts containing hair and sebaceous material (Figs. 5.9 and 5.10).

Patnaik *et al.* (1976) described malignant ovarian teratomas in a Bull Mastiff and a German Shepherd. The Bull Mastiff developed agalactia, listlessness, and fever following whelping. An abdominal mass was palpated and exploratory laparotomy revealed the presence of a 10-cm mass in the left ovary. The bitch recovered temporarily following ovariohysterectomy. Four months after surgery, the bitch was presented for examination because of listlessness, poor appetite, and neck pain. All peripheral lymph nodes were enlarged. A large mass was palpated in the vicinity of the left kidney. The bitch was killed and metastases of the ovarian teratoma were found around the left kidney, in the anterior mediastinum, in the lungs, and in the peripheral lymph nodes. The primary ovarian lesion consisted of large cysts containing keratin and sebaceous material and lined by squamous epithelium, hair follicles, and adnexal structures. Is-

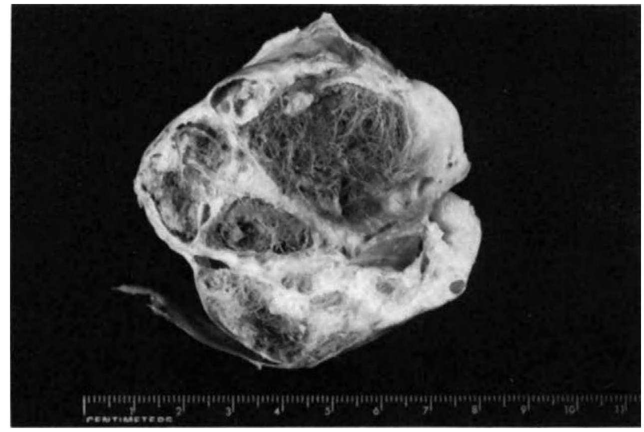

Fig. 5.9. Canine ovarian teratoma that measured 8 x 10 cm and contained hair, bone, adipose tissue, and smooth muscle. Acc. No. 18441.

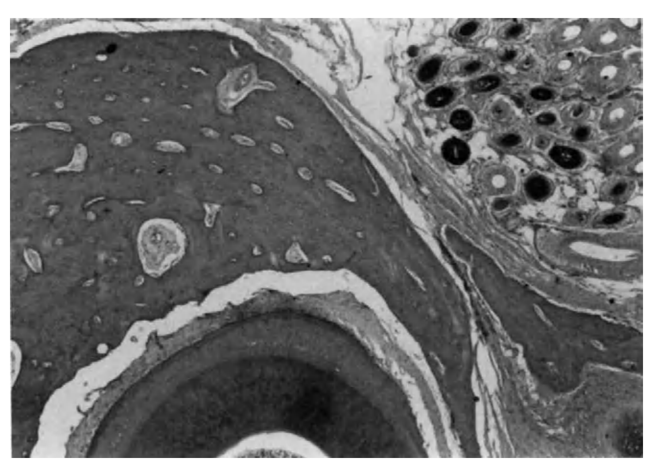

Fig. 5.10. Canine ovarian teratoma containing tooth, bone, and skin with adnexal tissues. ×30. Acc. No. 12068.

lands of myxomatous cells, spindle cells, and anaplastic epithelial cells were located between the cystic structures. The metastatic lesions were reported to be more bizarre than those of the primary lesion.

The 9-year-old German Shepherd was presented with a dry, nonproductive cough, foreleg lameness, and a recent onset of polyuria and polydipsia. Pain was evident upon palpation of the right elbow. Abdominal radiographs showed a large circumscribed midabdominal mass with numerous irregular foci of calcification. A large mass was found in the right ovary during surgical exploration. The bitch was ovariohysterectomized. The right ovary was 720 cm in volume and had a thick capsule and an irregular surface. The cross section was multilobed and consisted of solid and cystic areas. The tissues in the neoplasm included skin and adnexal structures, central nervous system tissue, skeletal and smooth muscle, lymphoid tissue, cartilage, and osteoid and acinar structures. Lameness persisted following surgery and palpation of the right stifle and right elbow elicited considerable pain. Radiographs revealed lytic lesions, suggestive of a metastatic neoplasm, in the right ulna and the olecranon process and the right tibial crest. A complete necropsy was not permitted but metastases of the ovarian neoplasm were found in the bones. The metastatic lesions in the bones consisted of "bizarre, large, spindle to polygonal cells, resembling mesenchymal cells. There were also other areas with equally anaplastic cells, forming glandular-like structures similar to those found in the primary."

A malignant ovarian teratoma, which I examined from a 2-year-old Doberman bitch, had features of the endodermal sinus tumor (Fig. 5.11) that occurs in women (Kurman and Norris, 1976; Teilum, 1976). The bitch had weight loss and a fetid vaginal discharge for about 50 days following breeding. Surgery revealed an exudate-filled uterus, a 10-cm mass in the left ovary, and greatly enlarged sublumbar lymph nodes. The bitch was killed and portions of the ovarian neoplasm and the enlarged lymph nodes were submitted for examination.

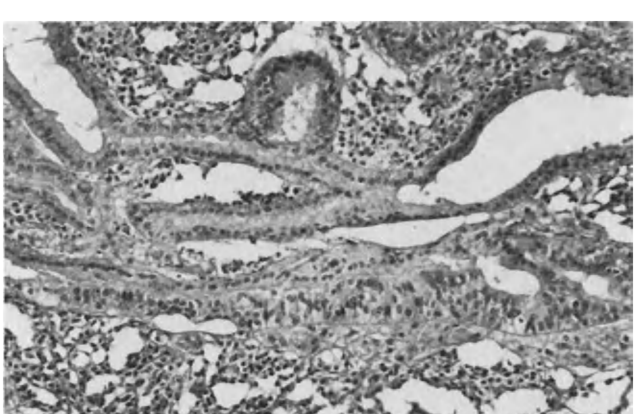

Fig. 5.11. Malignant canine teratoma with features of an endodermal sinus tumor. ×89. Acc. No. 17964.

The histologic appearance of the primary neoplasm and the metastatic lesions was similar. It was a solid, highly cellular neoplasm with large areas of necrosis, hemorrhage, and neutrophilic infiltration. The neoplasm consisted of a mixture of solid and reticular areas. The reticular areas consisted of a loose network of cavities and channels lined by flattened to cuboidal epithelial cells. The solid areas consisted of compact aggregates of undifferentiated embryonal cells, many of which resembled primordial germ cells. Mitotic figures were numerous. There were foci of cells with eosinophilic, heavily vacuolated cytoplasm. Nests and tubules of tall columnar epithelial cells were scattered throughout the neoplasm.

Alpha-fetoprotein has been demonstrated by the immunoperoxidase reaction in human endodermal sinus tumors (Kurman and Norris, 1976). The presence of the fetal antigen, alpha-fetoprotein, is indicative of a similarity of the tumor to yolk sac endoderm.

Intracranial germinomas in the dog have been reported by Dahme and Schiefer (1960) and Cordy (1984).

Cow. Dehner *et al.* (1970) reported ovarian teratomas in one Jersey and two Hereford cows. One neoplasm was described as large, and the other two weighed 5.7 and 13 kg. Metastases were present in the kidneys, uterus, and abdominal lymph nodes in the cow with the largest neoplasm. McIntosh (1949) recorded a 43.6-kg ovarian teratoma in a 15-month-old crossbred Hereford heifer. Portions of the intestine were firmly attached to the neoplasm.

Benign cystic ovarian teratomas (dermoid cysts) occur more frequently in zebu cows than in European breeds of cattle (Costa, 1974; Cotchin and Marchant, 1977). Dermoid cysts in zebu cattle are frequently multiple and bilateral. Vale *et al.* (1984) found ovarian teratomas in 38 animals in a series of 9517 crossbred zebu cows that were slaughtered in Belém, Brazil. The tumors were bilateral in 7 cows, located in the right ovary in 15 cows, and in the left ovary in 16 cows. Fifteen of the cows were pregnant. Granulosa cell tumors were diagnosed in 7 cows. This is in marked contrast to the occurrence of ovarian tumors in European breeds of cattle in which granulosa cell tumors occur much more frequently than teratomas.

The individual cysts vary in size up to 4 cm in diameter and contain thick milky or viscous fluid. The dermoids are scattered throughout the ovary and usually bulge above the surface. Multiple bilateral neoplasms may be present without interfering with ovarian function. The cysts are lined by stratified squamous epithelium with varied degrees of keratinization.

Areas of pseudostratified ciliated epithelium and goblet cells may be intermingled with the squamous epithelium. Other tissues may be present, including cartilage, salivary gland, central nervous system tissue, smooth muscle, adipose tissue, hair follicles, sweat glands, and sebaceous glands. The neoplasms are usually diagnosed only at slaughter.

Queen. Norris *et al.* (1969a) found two teratomas in a series of 11 ovarian neoplasms in domestic cats. A 1.5-cm benign cystic teratoma occurred in one ovary of a 2-year-old cat. A 6-year-old cat had a unilateral solid ovarian teratoma that weighed 1000 g. The latter tumor was diagnosed as a malignant teratoma with dysgerminoma. Mestastases were not found.

Gruys *et al.* (1976a) found a firm, gray-yellow, and partly necrotic teratoma around the aorta between the adrenal glands and in the pelvic inlet in a cat. A dysgerminoma was found in one ovary at surgery 3 months before. They proposed that the teratoma may have arisen in a metastasis from the dysgerminoma. Wilkinson *et al.* (1966) reported a dermoid cyst in the left ovary of a 6-month-old cat.

Sex Cord–Stromal Tumors

Granulosa Cell Tumor

The granulosa cell tumor is the most common ovarian neoplasm in the cow and the mare. Granulosa cell neoplasms and SES neoplasms occur with about equal frequency in the bitch.

In the series of 498 ovarian neoplasms that I have examined, 84 of 139 bovine tumors were diagnosed as granulosa cell tumors, 12 as thecomas, and 4 as luteomas. In the series of 276 canine ovarian neoplasms, there were 101 granulosa cell tumors, 8 thecomas, and 5 luteomas. The collection includes 52 equine ovarian neoplasms, 45 of which were granulosa cell tumors. No thecomas or luteomas were found in the mare. Nine of 22 feline ovarian neoplasms were granulosa cell tumors and 5 were interstitial gland tumors.

Cow. The granulosa cell tumor of the bovine ovary was reported first by Goldberg (1920). Baumann (1935) presented detailed descriptions of the gross and histologic features of six bovine cases from abattoirs. The largest neoplasm measured 48 x 38 x 19 cm and weighed 17.1 kg. No metastases were found in any of the cases. Zinnbauer (1961) reported a 40-kg granulosa cell tumor in the right ovary of an 8-year-old Fleckvieh cow. Arthur (1964) reported a 52-pound granulosa cell tumor that developed in a 3-year-old Friesian cow.

The age range of cattle with granulosa cell tumors in my series was newborn to 19 years with a median age of 7 years. This differs from Cotchin and Marchant's (1977) report that "the majority of tumors have been reported in animals of about two to three years of age."

Affected cows may manifest nymphomania, virilism, or be free of clinical signs. Granulosa cell tumors have been found in a few pregnant cows. Short *et al.* (1963) conducted an endocrinologic study of a granulosa cell tumor in a virgin Friesian heifer. The mammary glands began to enlarge when the heifer was about 2 years of age. The heifer frequently mounted other animals in the herd, developed a bull-like voice, and pawed the ground like a bull. The tail head was raised and there appeared to be thickening of the neck. At 2 years and 6 months of age, the udder was greatly enlarged and the teats were distended with milk. The left ovary was grossly enlarged and the right ovary was small and inactive. The reproductive organs were examined following euthanasia. The left ovary was 15 cm in diameter and nodular. Multiple cysts containing either blood or straw-colored fluid were present in the neoplasm. Samples of cyst fluid were saved for steroid analysis. The right ovary measured 2 x 1 x 1 cm and contained no follicles larger than 1 mm. The neoplasm appeared to be a typical granulosa cell tumor. There was a high rate of mitotic activity in the endometrium and hyperplasia of endometrial glands. The cyst fluid from the tumor "contained progesterone, 20B-hydroxy-pregn-4-en-one, possibly a trace of 17X hydroxyprogesterone, and oestradiol-17B." The comment was made that "The progesterone : estradiol 17B ratio was only 6 : 1, and yet the tumor appeared to have caused mammary development and lactation" (Short *et al.*, 1963).

Bosu (1977) conducted steroid analyses on peripheral blood plasma of a 10-year-old Holstein cow with a granulosa cell tumor. During 7 months following the last parturition, the cow was bred five times without conceiving. Following the last breeding, she exhibited frequent estrus. Per rectal palpation revealed that the left ovary was small and inactive and the right ovary was 20 cm in diameter and lobulated. Surgery was delayed for 3 months because the cow was producing about 45 kg of milk per day. Masculinization of the head, thickening of the neck and shoulders, and marked elevation of the tail head were evident. The cow had remained anestrus for a period of about 6 weeks prior to surgery. A number of blood samples were collected prior to and following surgical removal of the neoplasm. The tumor measured 50 x 22.5 x 33.5 cm and weighed 9.7 kg. The cut surface was solid, lobulated, and mostly gray-yellow with hemorrhagic areas. The "tumor was predominantly of the granulosa cell type although elements were also noted resembling theca cells" (Bosu, 1977). Plasma estrogen levels varied from 36 to 75 pg/ml before surgery and between 2 and 30 pg/ml following surgery. The plasma progesterone levels were less than 0.5 mg/ml in most of the presurgical samples. The plasma testosterone levels were between 54 and 130 pg/ml before surgery and 25 to 70 pg/ml following surgery. Estrus was detected 18 days after surgery and the remaining ovary developed cystic follicles. The cystic condition was treated and the cow subsequently conceived. According to the author, "the estrogen levels observed in the present case were higher than those reported in cows during the estrous cycle, cows with naturally occurring cystic follicular degeneration, and cows with experimentally induced cystic ovaries. The testosterone levels in the plasma of the cow before surgery were higher than those reported for the cow during the estrus cycle."

Rindi and Braca (1972) reported ovarian neoplasms in six nursing calves. The neoplasms were unilateral and grapefruit size or larger. Based on the description of the gross and microscopic lesions, it appears that the neoplasms were granulosa cell tumors. Three of the six neoplasms were believed to be hormonally active because of the increased volume and turgidity of the uterus and increased thickness of the uterine mucosa.

Kanagawa *et al.* (1964) reported a granulosa cell tumor in a full-term Holstein calf that required obstetrical assistance because of the extreme abdominal enlargement. The calf died within a few minutes after delivery. The abdominal cavity contained about 1.8 liters of turbid bloody fluid and clots. The left ovary measured 15.5 x 14.0 x 7.5 cm, weighed 700 g, and had a 12-cm rupture in its capsule. Multiple cysts were present on the cut surface and the stroma was comparatively soft. The cysts were lined by granulosa cells. Theca cells were prominent in some areas and other areas contained luteal cells. The authors diagnosed the case as a "granulosa cell tumor accompanied in part by theca cell tumor and luteoma."

Granulosa cell tumors in the cow are usually unilateral and the gross appearance varies considerably. The surface may be smooth or coarsely lobulated. The cut surface may be solid, consist predominantly of cysts of varied size, consist of a mixture of solid and cystic tissue, or consist of a single large cyst lined by slightly raised patches of yellow, orange, or red tissue. The solid areas may be gray-white, yellow, or orange and vary in consistency from soft to firm. Areas of hemorrhage and necrosis occur in large neoplasms.

Follicular, trabecular, and diffuse patterns of growth of the neoplastic granulosa cells may be present. Some neoplasms are composed entirely or predominantly of one pattern of growth, whereas other tumors have a mixture of patterns. The neoplastic cells usually bear a close resemblance to granulosa cells in a growing follicle. They have spherical to oval hyperchromatic nuclei, distinct nucleoli, and scant, eosinophilic cytoplasm.

Call–Exner bodies (named after Drs. Call and Exner, 1875) are numerous in newly forming tumors but less frequent in large ones. A Call–Exner body consists of a small cavity containing follicular fluid surrounded by radially arranged granulosa cells (Fig. 5.12). Granulosa cell tumors appear to arise either from anovular follicles and cords in the ovarian cortex or from medullary tubules. Call–Exner bodies occur frequently in these structures in aged cows (Yamauchi, 1963).

Norris *et al.* (1969b) presented clinical and pathologic data on 26 bovine ovarian stromal tumors and distinguished between those of granulosa type and sustentacular (Sertoli) type. Thirteen cases were of each type. The tumors having a granulosa cell pattern had a microfollicular pattern with the formation of cysts resembling mature follicles. Several mitotic figures were evident in most high-power fields. Nine of the 13 granulosa cell tumors had metastasized. The tumors with a sustentacular cell pattern had a tubular arrangement of neoplastic cells with connective tissue separating columns and cords of cells. Very few mitotic figures were present. Small areas of the typical granulosa cell pattern were present in 5 of the tumors with a predominantly sustentacular cell pattern. None of the tumors with a sustentacular cell pattern had metastasized. The authors concluded that granulosa cell tumors in the cow are highly malignant.

In my series of cases of bovine granulosa cell tu-

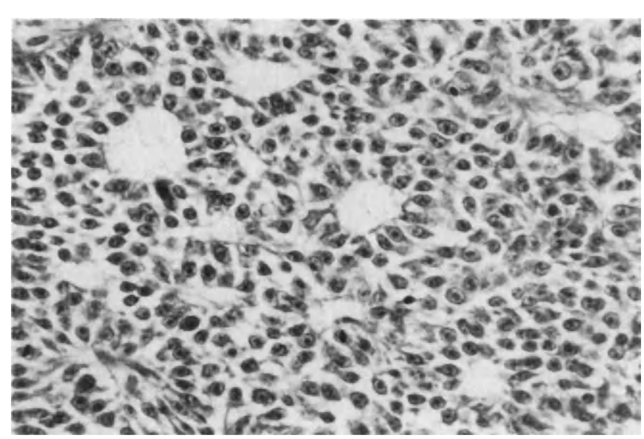

Fig. 5.12. Bovine granulosa cell tumor with Call–Exner bodies. ×222. Acc. No. 12284.

mors, very few were malignant. The difference in rate of malignancy might be accounted for by the possibility that both large ones and malignant neoplasms were more likely to be selected for submission to the Armed Forces Institute of Pathology, where the investigation was conducted. My cases were found during the examination of many thousands of bovine reproductive tracts over a period of more than 30 years. Many cases, particularly early ones, would have been missed during routine inspection in abattoirs.

Bitch. Cotchin (1961) reported 30 granulosa cell tumors in a series of 69 canine ovarian neoplasms. Nineteen of the 30 affected bitches had pyometra, 3 others had cystic endometrial hyperplasia, and 1 attracted male dogs for a period of 2 years. The neoplasms had smooth, nodular, or bosselated surfaces. The cut surface was gray, white, or yellow, moderately firm, and tended to contain cysts. Fibrous septa were variably developed. Two of the 30 granulosa cell tumors were malignant with extension to the pelvis and right kidney in one case and metastases in the sublumbar lymph nodes, liver, pancreas, and lungs in the other case. Approximately 50% of the granulosa cell tumors had a sustentacular (Sertoli) cell pattern.

Granulosa cell tumors in the dog appear to arise from granulosa cell cords derived from atretic follicles. The granulosa cells in these cords are elongated and have pale cytoplasm, resembling sustentacular cells. It is not surprising to find a sustentacular cell pattern in at least a portion of many canine granulosa cell tumors.

Norris *et al.* (1970) reported the clinical and pathologic features of 26 granulosa cell tumors in a series of 84 canine ovarian neoplasms. Fifteen of the neoplasms had a granulosa cell pattern, 6 had a sustentacular cell pattern, and 5 were classified as nonspecific gonadal stromal tumors. The latter group comprised neoplasms that could not be placed in the other two categories. Clinical signs and/or histologic lesions of hyperestrogenism were present in 5 of 15 dogs with granulosa cell pattern neoplasms, 3 of 6 with sustentacular cell pattern tumors, and 4 of 5 with nonspecific gonadal stromal tumors. Three (20%) of the neoplasms with a granulosa cell pattern had metastasized. There was no evidence of malignancy in the tumors with the other two cell patterns.

McCandlish *et al.* (1979) determined estrogen and progesterone levels in two bitches with granulosa cell tumors. The first case occurred in an 11-year-old West Highland White Terrier that had been in estrus for 9 months. The vulva was swollen and there was a hemorrhagic vaginal discharge. The bitch was attractive to male dogs but would not stand to allow mating. Blood samples were taken daily for 5 days for hormonal analysis. The estrogen and progesterone levels were comparable to those found in late proestrus. Following ovariohysterectomy, the blood levels of estrogen dropped to concentrations comparable to those seen in normal anestrous bitches. The vulva returned to normal size within 10 days following surgery.

The second case occurred in a 4-year-old Afghan bitch. Six months prior to presentation, megestrol acetate was used to suppress estrus, which had been apparent for 2 months. The bitch was presented for examination 4 days after the sudden onset of dullness and anorexia. Swelling and bleeding of the tongue developed on the second day of illness. The animal collapsed on admission. The heart rate was 140 per minute, the pulse volume was poor, and the mucous membranes were pale. There was marked swelling of the tongue, which was purple and oozed blood. Subcutaneous hemorrhage was present over much of the body. There was a blood-tinged mucoid vaginal discharge and the vulva was markedly swollen. A round mass was palpable in the midabdomen. Hematologic examination revealed "a moderately severe, non-regenerative anemia with agranulocytosis and absolute thrombocytopenia." Examination of the blood revealed abnormally elevated levels of estrogens and progesterone. The bitch was killed because of its very poor condition.

Unilateral, benign granulosa cell tumors were diagnosed in both cases. The first case had a microfollicular pattern and the second a sustentacular cell pattern. The nonneoplastic ovaries were inactive in both bitches.

Mare. Granulosa cell tumors in the mare are usually unilateral, multicystic, rarely malignant, and frequently accompanied by endocrine disturbances (Norris *et al.*, 1968; Cordes, 1969; Clark, 1975; Meagher *et al.*, 1977; Turner and Manno, 1983; McCoy, 1986). Forty-five of the 52 equine ovarian neoplasms that I have examined were granulosa cell tumors. The other equine ovarian tumors in my series included three dysgerminomas, two teratomas, one cystadenoma, and one malignant lymphoma.

Meagher *et al.* (1977) conducted a retrospective study of 78 cases of granulosa cell tumors in mares presented to the Veterinary Medical Teaching Hospital, University of California, Davis, California. The age range of affected mares was 2 to 20 years with a mean of 10.6 years. Clinical signs exhibited by affected mares included anestrus, continuous estrus, and stallionlike behavior. Some of the 29 mares showing a stallionlike behavior developed a heavy crested neck and heavy muscling in the forelegs and chest.

Two mares were pregnant at the time the tumors were diagnosed. Both mares successfully completed their pregnancies following surgical removal of the ovarian tumors.

The neoplastic ovaries were removed surgically from 77 of the 78 cases. Postsurgical complications occurred in 19 mares, of which 6 died. One mare was killed several months following surgery because of extensive abdominal metastases of the granulosa cell tumor. Following surgery, 59 of the mares returned to a normal temperament. "In seven cases the owners reported stallion-like behavior but in each case this was comparatively mild, with affected mares occasionally teasing other mares that were in estrus" (Meagher *et al.*, 1977). Thirty of 39 mares, known to have been bred postsurgically, produced live foals.

All the neoplasms were unilateral with approximately equal distribution between the right and left ovaries. The diameter of the neoplasms ranged from 6 to 40 cm with the majority between 10 and 20 cm.

The clinical, structural, and functional characteristics of granulosa cell tumors in 10 mares were reported by Stabenfeldt *et al.* (1979). Daily blood samples were obtained for a minimum of 3 weeks prior to surgical removal of the affected ovary and subsequently until the reappearance of cyclic ovarian activity. All tumors were similar in gross appearance. They ranged in size from 9 to 30 cm, weighed 1.5 to 6 kg, and were predominantly cystic with yellow stroma. No metastases were found. Granulosa cells lined the cysts (Fig. 5.13) and in other areas were arranged in trabecular cords and solid masses (Fig. 5.14). An irregular zone of thecal or stromal cells surrounded the granulosa cells. Large polyhedral, eosinophilic cells, which were referred to as "Leydig-like cells," were present in the stromal tissue in some tumors (Fig. 5.15). I believe they resemble luteal cells more closely than testicular interstitial cells. Stabenfeldt *et al.* (1979) reported the presence of "Leydig-like cells" in the theca of the granulosa cell tumors in 9 of the 10 mares: "All nine of these animals had higher than normal ($P < 0.005$) concentrations of testosterone in the peripheral plasma; 2 animals which exhibited male behavior had testosterone concentrations > 100 pg/ml and the largest number of Leydig-like cells in the theca." Estrogen concentrations were highest in the mare that had proliferation of "Sertoli-like cells" and lacked "Leydig-like cells." Mills *et al.* (1977) called an equine granulosa cell tumor with these cells an arrhenoblastoma (androblastoma). I have not seen an ovarian neoplasm in any species of domestic mammal resembling the androblastoma (arrhenoblastoma) of the human ovary.

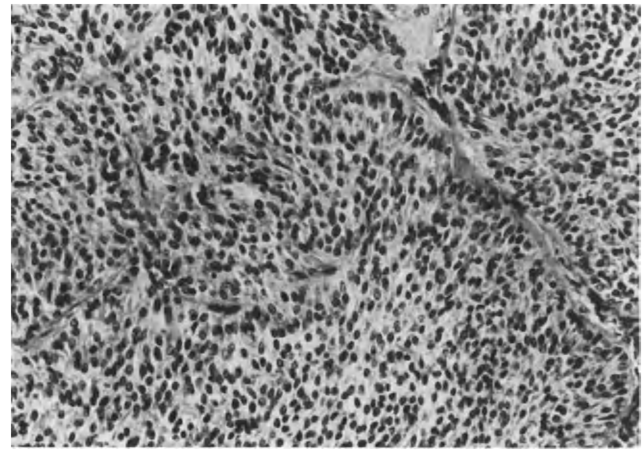

Fig. 5.14. Solid granulosa cell tumor from a mare. ×163. Acc. No. 18074.

Teige (1953) reported a case of pregnancy in a mare with a 13 × 10 × 8-cm cyst in one ovary. The cyst contained about 200 ml of thin, clear fluid. The cyst wall was composed of collagenous connective tis-

Fig. 5.13. Cystic granulosa cell tumor from a mare. ×163. Acc. No. 19261.

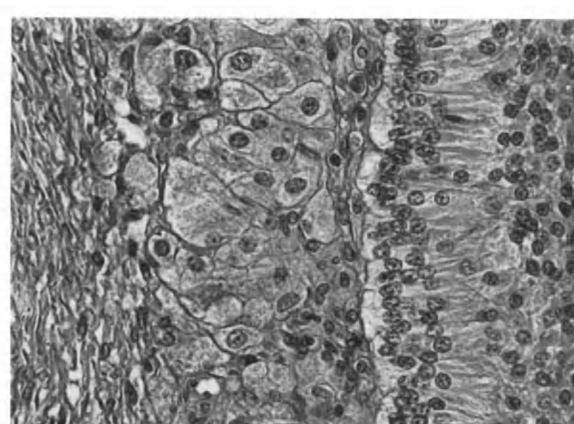

Fig. 5.15. Hypertrophic interstitial cells in stromal tissue of equine granulosa cell tumor. ×370. Acc. No. 1481.

sue with no epithelial lining. I have seen similar ovarian cysts in mares, cows, and bitches. Some of the cysts had small foci of slightly raised yellow tissue that were viable portions of granulosa cell neoplasms. The rest of the cyst wall was lined by collagenous connective tissue. These are granulosa cell tumors that have gradual destruction of the neoplasm by the proliferation of dense fibrous tissue in the cyst wall.

Hultgren *et al.* (1987) reported a granulosa cell tumor that occurred in the right ovary of a 3-month-old filly. The animal was killed because it had progressive abdominal distention, severe recurrent colic for 3 days, and intermittent diarrhea. The neoplastic ovary was twisted 360°, measured 32 × 27 × 27 cm, and weighed 7 kg. The abdominal cavity contained about 15 to 20 liters of red, cloudy fluid. The tumor had not metastasized and was probably present at birth.

Queen. Norris *et al.* (1969a) reviewed the literature on feline ovarian neoplasms and described 11 ovarian tumors from domestic cats. Granulosa cell tumors were found in five mature cats and signs of hyperestrogenism were evident in all five animals. Two had prolonged estrus with loss of hair and three others had cystic or adenomatous hyperplasia of the endometrium. The neoplasms were palpable in the abdomen of all five cats. The age range of affected cats was 3 to 16 years. Four of the neoplasms were unilateral and three were malignant. Bilateral granulosa cell tumors were present in one of the malignant cases. Metastases were found in the pelvic and abdominal peritoneum in three cats and in the lungs in one. The microscopic pattern was a microfollicular arrangement of granulosa cells. Call–Exner bodies were seen in two tumors. There was no evidence of luteinization. Mitotic figures and cellular atypism were prominent. They made the comment that "all our cat granulosa tumors appeared histologically malignant and their behavior appeared to be much more aggressive than that of similar tumors in human patients" (Norris *et al.*, 1969a).

Gelberg and McEntee (1985) reported granulosa cell tumors in 9 of 22 cats with ovarian neoplasms: "At least four of the cats with granulosa cell tumors demonstrated signs of abnormal estrus. Four of the tumors had metastasized." Histologically, the granulosa cell tumors had microfollicular and thecal or sarcomatous patterns. The neoplasms in two cats had areas of luteinization (Fig. 5.16).

Baker (1956), Engle and Brodey (1969), Aliakbrai and Ivoghli (1979), and Arnbjerg (1980) reported cases of malignant granulosa cell tumors in cats. The neoplasm reported by Arnbjerg apparently developed in an accessory ovary. A 5-year-old Siamese cat had weight loss for 6 months. A 4 x 3 x 3-cm granulosa cell tumor was located on the cranial end of the left uterine horn. There was no apparent connection to the left ovary. Both ovaries appeared normal and lacked grossly visible follicles and corpora lutea. No metastases were noted during surgery. The cat was normal for 7 months following surgery and then developed anorexia, vomition, emaciation, and depression. Multiple metastastic granulosa cell tumors were found in the liver, spleen, and kidneys. The peritoneum was normal and no metastases were found in the lungs.

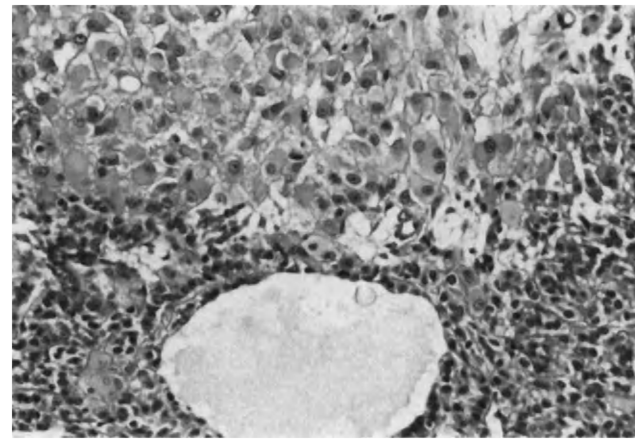

Fig. 5.16. Feline granulosa cell tumor with area of luteinization. ×178. Acc. No. 6985.

Sow. Nelson *et al.* (1967) conducted a survey to determine the incidence of ovarian neoplasms in 52,000 sows. They found one granulosa cell tumor, one papillary cystadenoma, and two hemangiomas. The granulosa cell tumor was bilateral. The right ovary was 20 cm in diameter and the left ovary 5 cm in diameter. The neoplasms were lobulated and gray and had large areas of necrosis, hemorrhage, and calcification. The neoplasms consisted of "polygonal epithelial cells arranged in large masses and in follicularlike and ductal structures" (Nelson *et al.*, 1967). The cells contained large round, vesiculated nuclei and abundant pale-staining, vacuolated cytoplasm. Mitotic figures were numerous.

Anderson and Sandison (1969) found one granulosa cell tumor in a 3-year-old sow. Metastases were present in the abdominal lymph nodes. One explanation for the low incidence of ovarian neoplasms in the sow is that most animals are slaughtered at a comparatively young age.

Ewe. Cordes and Shortridge (1971) reported three granulosa cell tumors in a series of 256 ovine neoplasms. The tumors were unilateral and occurred in a newborn lamb, a 9-month-old animal, and a 3-

month-old lamb that had bled to death following rupture of a 125-g tumor of the left ovary.

Goat. Lyngset (1963) described a large granulosa cell tumor in a goat and stated that it was not possible "to find any special mention of ovarian tumors in the goat in the literature."

Lofstedt and Williams (1986) reported a granulosa cell tumor that occurred in a 3-year-old Toggenburg goat. The doe had short estrous cycles and infertility followed by malelike behavior. "Before surgery, and at three and six days after tumor removal, serum testosterone concentrations were 0.05 ng/ml, 0.03 ng/ml and 0.02 ng/ml, respectively. At the same time, serum estradiol concentrations declined from 39 pg/ml to 23 pg/ml and 7 pg/ml, respectively, but serum progesterone concentrations increased from 0.12 ng/ml to 0.31 and 1.4 ng/ml" (Lofstedt and Williams, 1986). The tumor extract contained predominantly testosterone (20 ng/ml) followed by estradiol (10 ng/ml) and progesterone (1 ng/ml). The clinical signs of abnormal sexual behavior disappeared following surgical removal of the neoplastic ovary. The doe came into estrus and conceived 6 months following surgery.

Thecoma (Theca Cell Tumor)

Thecomas occur much less frequently than granulosa cell tumors in domestic mammals (Johnston, 1962; Tontis *et al.*, 1982). I have seen them in 12 cows, 8 bitches, and 1 sow. They are firm, solid, white, yellow, or orange neoplasms. Areas of necrosis and hemorrhage occur in the large neoplasms. Histologically the thecoma is characterized by masses of oval or spindle-shaped cells with pale streaming cytoplasm (Fig. 5.17). The cells are often arranged in interlacing fascicles. Lipid can be demonstrated in the cytoplasm of the neoplastic cells, and this feature is helpful in differentiating thecomas from fibromas. Some granulosa cell tumors have a sarcomatoid appearance and present a problem in differentiating them from thecomas. In these cases, the reticulum stain will show reticulum surrounding individual cells in the thecoma and not in the granulosa cell tumor.

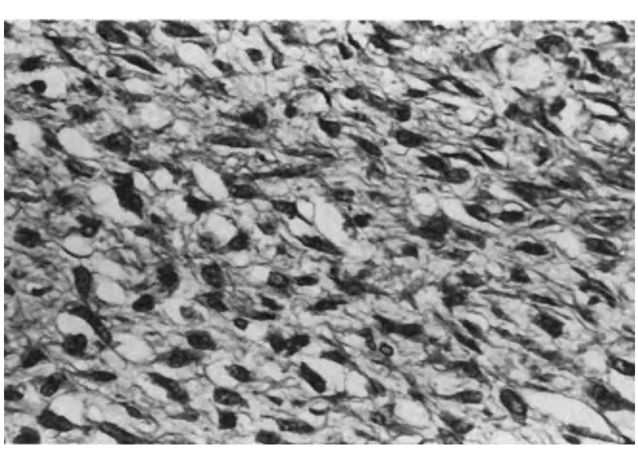

Fig. 5.17. Malignant thecoma from a 4-year-old cow. ×222. Acc. No. 15535.

Interstitial Cell Tumor (Luteoma, Lipid Cell Tumor)

In human pathology, the term luteoma appears to be used principally for the single or multiple nodules of large lutein cells that develop during pregnancy and regress thereafter. They are referred to as pregnancy luteomas (Scully, 1979). The term "lipid cell tumor" is used in human pathology for ovarian neoplasms composed of large, rounded, or polyhedral cells that resemble luteal, interstitial, or adrenal cortical cells but cannot be identified specifically as any one of the three. I have examined ovarian interstitial cell tumors from three cows, six bitches, and five cats.

Cow. The left ovary of a pregnant zebu cow measured 10.2 x 9.4 x 7.8 cm (reported by Costa, 1974). The neoplastic gonad had a smooth, slightly lobulated, highly vascular surface. The cut surface was orange and contained small cavities. The tumor consisted of dense sheets of irregular-shaped cells with abundant, finely vacuolated cytoplasm. The supporting tissue consisted predominantly of blood vessels.

One of my cases occurred in a 13-month-old Jersey heifer that died because of chronic pneumonia. The right ovary consisted of a rounded, 8 x 12-cm, firm mass. A 6-cm, bright orange structure was noted on the cut surface. Large blood vessels occupied the rest of the ovary. The orange tissue consisted of large cells with abundant, finely vacuolated cytoplasm. The rest of the gonad consisted of a vascular hamartoma.

The third interstitial cell tumor was found in a 7-year-old Holstein cow. The ovary measure 4.5 x 4 x 4.5 cm and weighed 31 g. A 1.5 x 2-cm regressing corpus luteum and a 3 x 3-cm pale gray neoplasm were present in the enlarged ovary. The neoplasm consisted of nests of luteal-appearing cells in a modest amount of connective tissue stroma.

Bitch. Ovarian interstitial cell tumors were found in six bitches between the ages of 5 to 14 years. All the neoplasms were unilateral and benign. A history of persistent vaginal discharge and/or swollen vulva was reported for three of the dogs. The largest tumor was 3.8 x 2.8 x 2.2 cm and the smallest was 8 x 6 mm. Since the tumors are relatively small, they can be overlooked easily during clinical or postmortem examination. The neoplasms arise from granulosa cell cords (Figs. 5.18 and 5.19). The neoplastic cells have

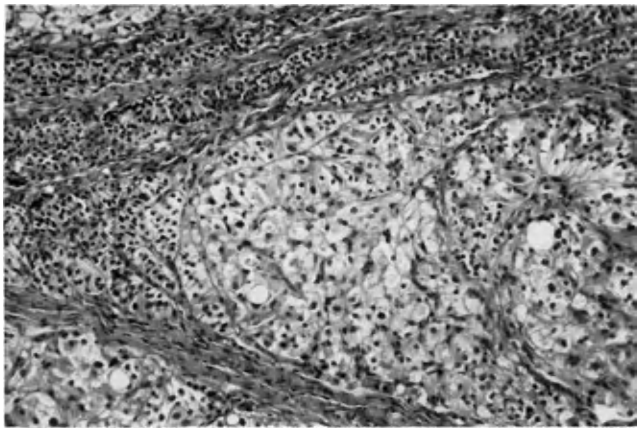

Fig. 5.18. Canine interstitial cell tumor developing in a granulosa cell cord. ×89. Acc. No. 16390.

abundant, finely vacuolated cytoplasm (Fig. 5.20) that is laden with lipid. Blood vessels are the predominant supporting tissue.

Queen. Gelberg and McEntee (1985) reported five cases of interstitial gland (cell) tumors in cats. The tumors consisted of solid, orange-yellow to brown masses of tissue. The largest tumor measured 5.1 x 3.6 cm (Fig. 5.21). "These tumors were composed of a homogeneous population of large distinctly bordered polyhedral cells with variably sized round central nuclei. The cytoplasm contained single large to multiple small, clear vacuoles. Some cells contained brown amorphous pigment. A fine fibrovascular stroma separated the cells into lobules" (Gelberg and McEntee, 1985).

Norris *et al.* (1969a) reported a lipid cell tumor in a 9-year-old domestic cat that had prolonged estrus, enlargement of the head and neck, a lowered voice,

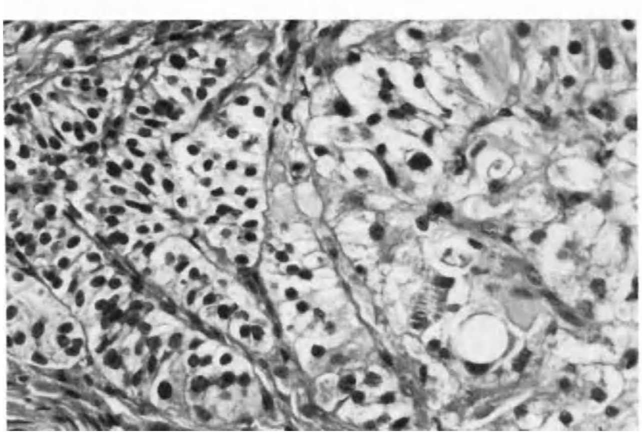

Fig. 5.19. Canine interstitial cell tumor developing in a granulosa cell cord. ×222. Acc. No. 16390.

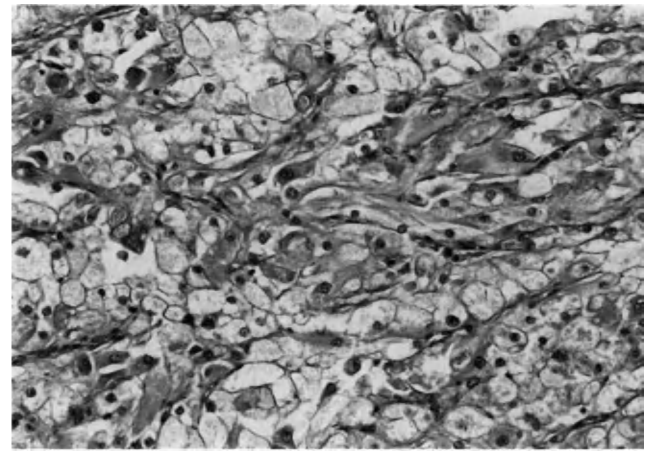

Fig. 5.20. Canine interstitial cell tumor. ×163. Acc. No. 16621.

and an increase of nocturnal activity. A benign ovarian cyst and a 1.5-cm gray, solid nodule were found in one ovary. The tumor consisted of a relatively uniform population of round cells with well-defined cytoplasmic margins. The cytoplasm varied from granular and eosinophilic to light and foamy. The histologic appearance of the neoplasm was similar to those called interstitial gland tumors.

Androblastoma (Sertoli–Leydig Cell Tumor, Arrhenoblastoma)

The term androblastoma (Sertoli–Leydig cell tumor, arrhenoblastoma) is mentioned because some ovarian neoplasms in the cow, mare, ewe, and queen have been reported as either arrhenoblastomas or androblastomas. According to the "Histological Typing of Ovarian Tumors," published by the World Health

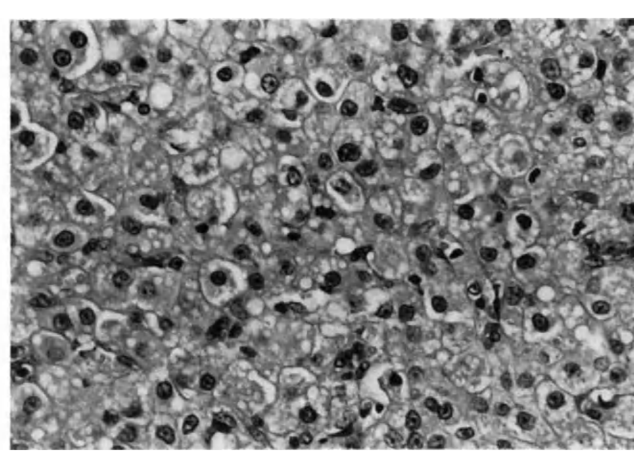

Fig. 5.21. Feline interstitial cell tumor. ×370. Acc. No. 19457.

Organization, the term arrhenoblastoma is inappropriate "because it carries the connotation of masculinization (Servo *et al.*, 1973). The terms androblastoma and Sertoli–Leydig cell tumor are used widely and are listed as alternatives in the WHO classification of ovarian neoplasms" (Scully, 1979).

According to Teilum (1976), "The designation 'androblastoma' (from *andros* meaning man) emphasizes the histological and histogenetic unity of tumors in either sex derived from the mensenchymal core which histologically reflects various phases in the development of the male gonad." For an explanation of the histogenesis of the androblastoma, it has been assumed that primary sex cords are associated with the development of seminiferous tubules and that persisting remnants (medullary cords) in the medulla of the ovary are the source of androblastomas. This theory may be incorrect if it is accepted that ovarian follicles and seminiferous tubules develop from an undifferentiated blastema in the center of the embryonic gonad. Medullary cords and tubules are present in the ovaries of all domestic mammals and it does not seem logical to assume that these are male structures. Jenson and Fechner (1969) studied the ultrastructure of a human ovarian "Sertoli–Leydig" cell tumor and concluded that the term was a histogenetic misnomer. Scully (1979) reviewed the theories of histogenesis of this tumor and proposed that "A more attractive hypothesis is that Sertoli–Leydig cell tumors arise directly from female cellular elements."

The equine "arrhenoblastoma" reported by Mills *et al.* (1977) has been mentioned in the discussion of granulosa cell tumors of the equine ovary. I consider this to be a form of the equine granulosa cell tumor in which there is hypertrophy of thecal elements.

Hofmann *et al.* (1980) reported a benign "androblastoma with Sertoli–Leydig cell pattern" in a 6-year-old domestic cat. The right ovary measured 7.5 x 5.4 x 3.6 cm and consisted of solid white and cystic areas. The left ovary was small and inactive. "The neoplastic cells were cuboidal or polygonal and were arranged in either trabeculae, strands with orderly whorls or tubular formation" (Hofmann *et al.*, 1980). The cysts were lined by cuboidal or columnar cells. There were groups of polygonal cells with eosinophilic, homogeneous cytoplasm. A few mitotic figures were present. There was adenomatous hyperplasia of the endometrium.

I have seen three feline ovarian neoplasms which were similar to the one described by Hofmann *et al.* (1980). The neoplasms consisted of closely packed cords and tubules of cuboidal to polygonal epithelial cells with a delicate network of supporting connective tissue. Cysts of varied size were scattered through the neoplasm and were lined by one to several layers of cuboidal to columnar cells. There were individual cells and clusters of large cells with abundant eosinophilic cytoplasm that was vacuolated in some areas. The numbers of these large cells, which closely resembled luteal cells and not interstitial (Leydig) cells, varied from scant to numerous in individual neoplasms. There appeared to be a transition from the cuboidal tubular cells to those resembling luteal cells. I prefer to call these neoplasms granulosa cell tumors with interstitial gland transformation.

Mesenchymal Tumors

Hemangioma

The hemangioma is the most common ovarian neoplasm in mature and aged sows. Laszlo (1940), Nelson *et al.* (1967), Maeda *et al.* (1972), Hsu (1983), and Silva *et al.* (1984) have reported ovariam hemangiomas in swine. These tumors occur rarely in the cow, mare, and bitch.

Ovarian hemangiomas may be unilateral or bilateral in the sow. The neoplasm consists of single or multiple masses of red-brown, spongy tissue that sometimes resembles testis on gross examination. The neoplasm consists of masses of small, very cellular blood vessels separated by bands of collagenous connective tissue. The vessels are lined by a single layer of endothelial cells and have large lumina in the center of the neoplasm and small lumina in the periphery. The histologic appearance of these neoplasms is somewhat suggestive of blood vessels in a regressing corpus luteum of pregnancy (Fig. 5.22). Hsu described an early porcine hemangioma that was found in the remnants of a degenerate corpus luteum. If this is the origin of these hemangiomas it would be of interest to determine why they occur more frequently in swine than in other species of do-

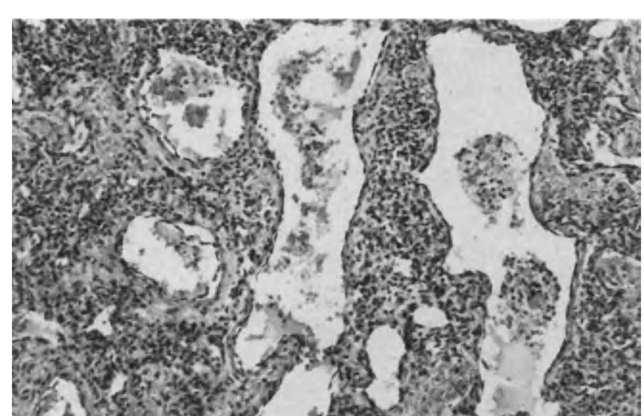

Fig. 5.22. Hemangioma in a porcine ovary. ×89. Acc. No. 18442.

mestic mammals. Possibly the neoplasms are induced by an angiogenic factor produced by the corpus luteum (Gospodarawicz and Thakral, 1978).

Akkermans and van Beusekom (1984) found this lesion in one ovary of 53 sows and in both ovaries of 3 animals during the examination of 1445 sows of relatively old age (mean parity of 6.8). The affected sows had a parity of 9.0. They reported the abnormal growths as "tumor-like lesions" because they considered that there were areas of granulosa cells among the proliferating blood vessels. I believe that the areas that they considered to consist of granulosa cells are foci of capillaries, fibroblasts, and macrophages. These foci may be remnants of degenerate corpora lutea.

Gruys *et al.* (1976b) reported a metastatic hemangiosarcoma in the left ovary of a 14-year-old mare that had severe dyspnea and died.

Leiomyoma

Leiomyomas develop from smooth muscle in the mesovarium. I have seen eight cases in the bitch and one in a queen. Most were found as incidental lesions. Anderson and Sandison (1969) reported a leiomyoma in the ovary of a sow. Nelson and Kelley (1971) and Nelson *et al.* (1972) found mesovarial leiomyomas in rats treated for several months with soterenol hydrochloride and mesuprine hydrochloride. These drugs are beta-adrenergic receptor stimulants and are related by chemical structure and pharmacologic activity.

Fibroma

Pure fibromas rarely occur in the ovary of domestic mammals. They arise from ovarian stromal cells and are closely related to thecoma. On the basis of an ultrastructural study, Amin *et al.* (1971) reported that "the ovarian fibroma and thecoma are not two different neoplasms but are variants of a single neoplasm with a common origin from the ovarian stroma."

Lymphoma (Lymphosarcoma)

Lymphoid tumors of the ovary are usually part of systemic lymphosarcoma. I have found that it is not unusual for this neoplasm to invade the corpus luteum of cattle (Fig. 5.23). Lock and Macy (1979) reported an ovarian lymphosarcoma in a 10-year-old Quarter Horse that had become weak and emaciated over a 4-month period of time. Neufeld (1973) found one case of a lymphoid tumor of the ovary during a review of 54 equine cases of lymphosarcoma. I have seen one case of lymphosarcoma of the ovary and uterus in a mare. The incidence of lymphosarcoma in the ovary

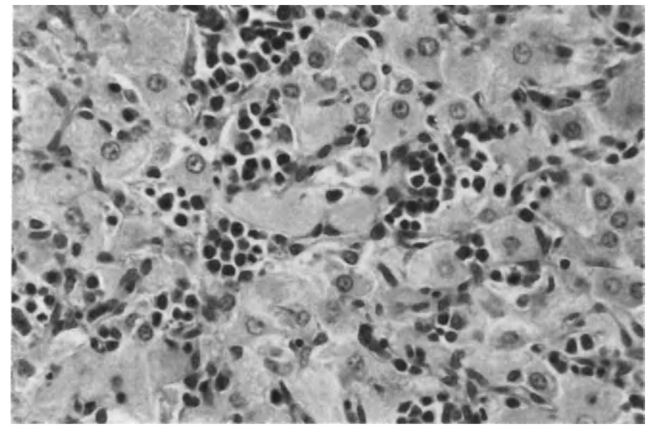

Fig. 5.23. Lymphosarcoma in a bovine corpus luteum. ×222. Acc. No. 18907.

would probably be found to be higher if the ovaries were examined histologically in all cases of lymphosarcoma.

Secondary (Metastatic) Tumors

From the paucity of reports, one might think that metastases to the ovary are rare in domestic mammals. However, the ovaries of animals are seldom examined histologically in case of malignant neoplasms of other organs. Therefore, the actual incidence of metastatic neoplasms in the ovaries of domestic animals has not been determined. Malignant lymphomas are found most frequently in the ovary of the cow and bitch, mammary carcinomas in the bitch, and uterine carcinomas in the cow. Malignant intestinal carcinomas, bile duct carcinomas, and pancreatic carcinomas have been found occasionally in the ovary. When examining ovaries for metastatic lesions, particular attention should be paid to corpora lutea. In the bitch I have found metastatic lesions of a malignant melanoma and a mammary gland carcinoma (Fig. 5.24) in luteal tissue.

Tumorlike Lesions

Adenomatous Hyperplasia of the Rete Ovarii

Hypertrophy and hyperplasia of the rete epithelium occur in aged dogs and may be a preneoplastic lesion. Anderson and Simpson (1973) reported that hyperplasia of the rete ovarii occurs frequently in aged Beagles.

Papillary Hyperplasia of Ovarian Serosa

The administration of stilboestrol to dogs causes papillary outgrowths from the ovarian surface epithe-

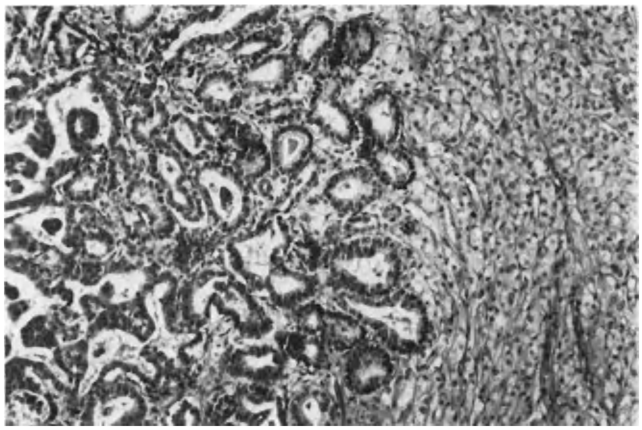

Fig. 5.24. Mammary gland carcinoma in a canine corpus luteum. ×89. Acc. No. 19575.

lium. These ovarian proliferations "were seen in a mild form after a short period (37 days) of stilboestrol administration, regressed following hormone withdrawal and never led to enlargement of the ovary beyond a diameter of 2 cm" (O'Shea and Jabara, 1967).

Stromal Hyperplasia and Hyperthecosis

The term stromal hyperplasia denotes a nonneoplastic proliferation of ovarian stroma. Stromal hyperthecosis refers to the presence of clusters of lutein cells in a stroma that is usually hyperplastic (Scully, 1979). These conditions have apparently been overlooked in veterinary pathology because no reference to them in domestic mammals has been found in the literature.

I have seen ovarian stromal hyperplasia in aged cattle and goats, and it is quite likely that it will be found in other species of domestic mammals when ovaries are examined from a large number of aged animals. The lesion is in the cortex and consists of multiple irregular-shaped masses of plump stromal cells with an increased amount of rather clear cytoplasm. One case in a goat had multiple small nodules of luteal tissue in addition to focal proliferation of stromal cells.

Vascular Hamartoma

Hamartomas are tumorlike malformations of tissue indigenous to the area. The common red birthmark of human beings is an example of a well-recognized vascular hamartoma. They are present at birth and usually regress or remain static unless they become traumatized or infected. Vascular hamartomas of the ovary have been reported in the bovine, porcine, and equine species (McEntee, 1965; Lee and Ladds, 1976; Rhyan *et al.*, 1981).

I have seen 11 ovarian vascular hamartomas in cattle. One case was found in a term fetus. The right ovary was about 17 cm in diameter, soft, and red. Another case was found in a 3-month-old calf. The right ovary measured 5 x 3 x 2 cm. The cut surface revealed a dense mass of firm tissue with multiple, blood-filled cystic spaces about 5 mm in diameter. Several small areas of pale yellow and dark orange tissue 2 to 3 mm in diameter were present. Histologic examination revealed the presence of numerous mature-appearing blood vessels in a fibrous tissue stroma. The "cysts" noted on gross examination were lumina of blood vessels. The yellow and orange foci were nests of neoplastic granulosa cells. Granulosa cell tumors were found in association with vascular hamartomas in two other cases and a luteoma was found in one case.

The rest of the bovine ovarian vascular hamartomas were found in adult cattle. In adult cattle, the vascular hamartomas ranged in size from 1 cm in diameter to a mass weighing 32.7 kg. The smaller growths consisted of intertwining masses of mature-appearing arteries and veins with a modest amount of supporting connective tissue. The largest hamartomas were coarsely lobulated and replaced most or all of the gonad. The amount of dense fibrous tissue increased proportionally with increase in size of the hamartoma. The increase in size of the vascular hamartoma in mature animals appeared to have been the result of thrombosis of the long, tortuous vessels with subsequent edema, hemorrhage, and necrosis followed by proliferation of fibrous connection tissue. Considering the complex vasculature of the ovary, it is surprising that vascular malformations do not occur more frequently.

Ovarian Cysts

The 16 types of cysts that are found in and around the ovaries of domestic mammals are discussed in Chapter 4.

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Chapter 6

The Uterine Tube

Anatomic Features
- Cow
- Ewe and Goat
- Sow
- Mare
- Bitch
- Queen

Minor Congenital Anomalies
- Accessory Funnels
- Accessory Uterine Tube (Appendix Vesiculosa, Hydatid of Morgagni)
- Cystic Remnants of the Mesonephric Duct
- Ectopic Adrenal Cortical Nodules

Major Congenital Anomalies
- Agenesis
- Segmental Aplasia
- Accessory Ostium
- Duplication
- Diverticula

Salpingitis
- Cow
- Ewe
- Sow
- Mare
- Bitch and Queen

Acquired Cysts
- Intraepithelial Cysts
- Cystic Epithelial Recesses

Squamous Metaplasia

Adenomyosis

Neoplasms

Bibliography

Anatomic Features

Gabriel Fallopius described the mammalian uterine tube in 1561 (Woodruff and Pauerstein, 1969). The term *oviduct* is used commonly in veterinary medicine and the term *Fallopian tube* in human medicine to denote the uterine tube. The term *uterine tube,* rather than oviduct, should be used for the tubular structure leading from the ovary to the uterus in domestic mammals. The term *oviduct* refers to the entire reproductive tract from the ovary to the cloaca of submammalian species.

The uterine tube is divided into four anatomic segments: infundibulum, ampulla, isthmus, and uterotubal junction. The infundibulum is a funnel-shaped expansion of the ovarian end of the tube. A portion of the infundibulum is attached to the tubal pole of the ovary. The ampulla forms the proximal two-thirds of the tube and is relatively wide. The isthmus is the narrow part of the tube proximal to the uterotubal junction. The uterotubal junction is the area of transition from the tube to the uterus.

The wall of the uterine tube consists of three layers: mucosa, muscularis, and serosa. The muscularis increases in thickness from the infundibulum to the uterotubal junction. It consists of a well-defined inner circular layer and a thin longitudinal outer layer. The mucosa has longitudinal folds projecting into the lumen. The mucosal folds are tall and have secondary and tertiary folds in the infundibulum and secondary folds in the ampulla. The longitudinal folds are short, few in number, and lack secondary folds in the isthmus. The mucosa consists of a lamina epithelialis and a lamina propria that has no glands. There are epithelial-lined recesses of the lumen in the lamina propria of the uterine tube in the dog and cat. These structures resemble glands and are found in the infundibulum and ampulla. The tubal mucosa has four types of epithelial cells: ciliated cells, secretory cells, basal cells, and peg cells (which are considered to be exhausted secretory and basal cells). The uterine tube is enclosed in a peritoneal fold, the mesosalpinx. The ovarian bursa is formed between the mesosalpinx laterally and the proper ligament of the ovary, mesovarium, and ovary medially.

The comparative morphology and the function of the uterine tube have been reviewed by Hafez and Blandau (1969), Johnson and Foley (1974), and Hunter (1977). Schilling (1962) described the structure and function of the uterine tube in cattle and sheep. Stalheim *et al.* (1975) described the luminal surface topography of bovine, equine, and caprine uterine tubes as viewed by scanning electron microscopy.

In most mammals, the transport of ova through the uterine tube requires about 3 to 5 days. The passage time is 6 to 8 days in the bitch, 5 to 9 days in the queen, and 2 to 3 days in the sow. There is rapid passage through the ampulla to the ampulla–isthmus junction, where a delay enables fertilization and early embryonic development to occur. Following the delay, the zygote passes rather rapidly to the uterus (Holst and Braden, 1972).

Cow

Drennan and Macpherson (1966) reported that the mean length of the right uterine tube of heifers is 16.45 cm and the left is 16.72 cm. The uterine tube in the cow is 20 to 35 cm long. The isthmus comprises one-third to one-half of the tube. The diameter of the isthmus ranges from 1 to 3 mm and the ampulla from 3 to 5 mm. Lombard *et al.* (1950) described the morphology of the uterine tube in virgin heifers in relation to the estrous cycle. They reported that "the mucosa of the oviduct formed folds with four to eight rugae at the uterine extremity and became more numerous toward the ostium abdominale. As high as 40 folds have been observed in one organ."

The ovarian bursa is wide and deep in the cow. The uterine tube can be palpated on per rectal examination in the cow by holding the ovary between the thumb and the third finger and slipping the first two fingers into the ovarian bursa (Williams, 1924). The uterine tube can then be palpated between the fingers and the thumb. In adult cows, it is usually necessary to release the ovary to allow the fingers to reach the depth of the bursa.

The fimbriated portion of the infundibulum is large enough to cover the ovary at the time of ovulation. The opening of the normal tube is directly opposite the mature follicle at the time of ovulation (Schilling, 1962). Fluid secreted by the uterine tube flows toward the abdominal ostium when the cow is under the influence of estrogen, so ligation of the infundibulum during estrus results in distention of the uterine tube. The distention is maintained for about 72 hours after ovulation. Black and Davis (1962) demonstrated that the blockage is due to contraction of the isthmic musculature and not to the presence of the tubouterine junction. The uterine tube still became distended with fluid when the infundibulum was ligated and the isthmic end of the same tube was severed approximately 1 cm anterior to the tubouterine junction. Spermatozoa, however, are able to ascend the uterine tube during this time, even though it is blocked to the passage of fluid (Edgar and Asdell, 1960).

A marked flexure of the uterine tube is present at the uterotubal junction in the cow. The opening of the uterine tube into the uterus is smooth and funnel-shaped with no special projections of the tubal mucosa into the uterine lumen.

McDaniel *et al.* (1968) investigated the influence of ovarian hormones on the histology and histochemistry of the bovine uterine tube. They reported that the nuclei of nonciliated cells are extruded under the influence of progesterone. The extruded nuclei were most numerous in the upper ampulla.

Ultrastructural and ultracytochemical changes in the epithelium during the estrous cycle of the bovine uterine tube were reported by Nayak and Ellington (1977). Maximum secretory cell differentiation was apparent during the follicular phase of the estrous cycle. Cytoplasmic protrusions were prominent during the luteal phase and extruded nuclei were present in the tubal lumen. Cilia were present in the tubal lining epithelium throughout the cycle and degeneration of cilia was not observed.

DuBois *et al.* (1980) determined the tissue concentrations of mast cells and lymphocytes in the ampulla and isthmus of the bovine uterine tube during the estrous cycle. The mast cell count was found to be significantly higher in the isthmus than in the ampulla for all stages of the estrous cycle. Mast cell numbers increased significantly during metestrus, diestrus, and proestrus in the isthmus and during metestrus and diestrus in the ampulla. "The lymphocyte numbers remained relatively constant in both the ampulla and the isthmus except during diestrus, when ampullary lymphocyte numbers increased significantly ($P < 0.05$). Lymphocytes were observed to migrate through the uterine tube epithelium and mast cells were observed only in the lamina propria" (DuBois *et al.*, 1980). Nellor (1965) suggested that the primary function of lymphoblastlike cells is to increase these cells before estrus and that the cells may be involved with bactericidal activity in the uterine tube during estrus. It has also been proposed that the lymphocytes may be involved in an immunologic response.

Ewe and Goat

The morphology of the uterine tubes of the ewe and goat is similar to that of the cow. The length of the ovine uterine tube is 15 to 20 cm. The uterine tubes of sheep may be gray or black because of the presence of melanin pigment. The uterine glands do not end abruptly at the tubouterine junctions but are present for a few millimeters anterior to the uterus.

Abdalla (1968) recorded the morphologic changes and histochemical findings in the uterine tube of sheep during pregnancy and various stages of the estrous cycle. Willemse (1975) conducted a detailed study of the hormonal control of the secretory activity of the epithelium of the ampulla of the uterine tube in the ewe. Nayak *et al.* (1976) described the cyclic ultrastructural changes in the infundibulum of the uterine tube in the ewe.

Sow

The uterine tube in the sow is 15 to 30 cm long. The infundibulum is large and completely covers the ovary at the time of ovulation. The isthmus is almost straight but has a slight flexure at the uterotubal junction. Fingerlike projections of the mucosa extend into the uterine lumen at the tubouterine junction (Lee, 1928; Rigby and Glover, 1965).

Mare

The uterine tube of the mare is 20 to 30 cm long and runs a tortuous course in the mesosalpinx. The fimbria of the infundibulum cover the ovulation fossa during ovulation. The lumen of the uterine tube communicates with the uterus through a small opening in the center of a small papilla that projects into the uterine lumen.

In the mare, unfertilized ova are retained in the uterine tubes for months, whereas fertilized ova pass into the uterus. It has been estimated that ova may be retained and remain identifiable in the mare for as long as 7½ months (van Niekerk and Gerneke, 1966). Similar retention of ova in the uterine tube has not been reported in other species of domestic mammals. Steffenhagen *et al.* (1972) reported that the mean number of ova recovered per mare was 3.3 for 17 nonbred mares and 1.9 for 32 bred mares, and "the retention of ova occurred primarily in the middle one-third of the uterine tubes in both bred and nonbred mares." The mechanisms involved in the retention of ova in the mare have not been determined definitely. Onuma and Ohnami (1975) stated that "globular masses, probably consisting of desquamated tubal mucosa, were frequently lodged in the distal region of the ampulla and appeared, to some extent, to cause the retention of more eggs." Tsutsumi *et al.* (1979) stated that "the results of the present study clearly show that the masses originate from the oviductal mucosa. However, the process of formation and the functional role of the masses are still unknown."

Bitch

The uterine tube of the Beagle bitch is about 6 cm long, takes a tortuous course in the mesosalpinx, and almost completely encircles the ovary. The mesosalpinx completely encloses the ovary except for the narrow entrance to the ovarian bursa (bursal slit). During estrus a small red mass of tissue measuring about 2 × 5 mm (in the Beagle bitch) protrudes from the bursal slit. This is a portion of the fimbriae of the infundibulum that becomes hyperemic and edematous during estrus. The bursal slit becomes almost completely closed during anestrus so that fluid injected into the bursa expands the mesosalpinx rather than escaping into the peritoneal cavity (Andersen and Simpson, 1973). The mesosalpinx of adult, well-nourished dogs contains abundant adipose tissue so that the ovary is hidden almost completely except for a small area of the dorsomedial wall of the bursal sheath that is free of fat.

Verhage *et al.* (1973a) studied the epithelium of the ampulla of the canine uterine tube by light and electron microscopy during representative stages of the estrous cycle. During anestrus and early proestrous, the epithelium consists of uniformly staining cuboidal cells with a relatively low nuclear and cytoplasmic volume. Lighter-staining ovoid ciliated cells constitute less than 1% of the epithelial cell population. Hypertrophy and early cytodifferentiation are evident in the epithelial cells by mid-proestrus, and by later proestrus hypertrophy and cytodifferentiation are advanced. Ciliated cells differentiate and become mature more quickly than the nonciliated cells. Sixty percent of the epithelial cells have cilia at proestrus. By early estrus the ciliated cells are tall and columnar and possess an apical nucleus and a large amount of basal cytoplasm. The secretory cells do not reach maximum hypertrophy until midestrus.

During the early stages of metestrus, the process of regression and dedifferentiation begins, and by mid-metestrus the epithelial cells are similar to the basal cells observed during proestrus. The process of dedifferentiation continues at a declining rate during late metestrus and during anestrus. "No cellular extrusion or desquamation was observed during dedifferentiation as has been reported to occur in the bovine oviduct" (Verhage *et al.*, 1973a). They concluded that "during the estrous cycle of the bitch the epithelial basal cells of proestrus differentiate into either a ciliated or secretory cell and through the process of dedifferentiation return to the basal state by the end of anestrus."

Queen

In contrast to the bitch, the mesosalpinx of the queen does not contain adipose tissue and the ovary is only partially enclosed in the ovarian bursa. The uterine tube of the queen is 5 to 6 cm long. It opens into the uterus through a low papilla that protrudes into the uterine lumen. Verhage and Brenner (1975) studied estradiol-induced differentiation of the uterine tube epithelium in the cat. They demonstrated that 17B-estradiol restores the tubal epithelium of the ovariectomized cat to a fully differentiated state. They reported that "the mode of basal body and cilia formation is essentially the same as in the oviducts of various other species."

Minor Congenital Anomalies

Minor congenital anomalies, which do not interfere with function of the uterine tube, are common in all species of domestic mammals. Major congenital malformations, which cause reproductive problems in animals, are rare.

Accessory Funnels

Accessory funnels (infundibula) occur in all species of domestic mammals. They are miniature infundibula with a mucosa and muscularis similar to that of the main infundibulum. They may be open on one or both ends or may be closed on both extremities. Closed accessory funnels gradually become filled with a clear serous fluid. Cystic accessory funnels do not become as large as accessory uterine tubes. Consequently they are frequently overlooked.

Accessory Uterine Tube (Appendix Vesiculosa, Hydatid of Morgagni)

Felix (1912) distinguished between accessory uterine tubes and accessory funnels. He stated that accessory uterine tubes are "usually situated more caudally than the accessory funnels, and what is characteristic, they never unite with the principal funnel or principal tube; they end blindly after a short course."

The accessory uterine tube (hydatid of Morgagni) is also known as the appendix vesiculosus. It develops in the embryo at the extreme cephalic end of the paramesonephric duct and persists postnatally as a stalked vesicle attached to the caudal portion of the uterine tube. It may consist of a series of linear cysts or a single prominent cyst (Fig. 6.1). It has been suggested that some of the larger cysts may cause infertility in the mare (Archbald *et al.*, 1974).

Bransilver *et al.* (1973) stated that the fine structure of the paramesonephric appendages (hydatids of Morgagni) and the mesonephric duct and tubular remnants is quite different. The paramesonephric remnants bear a close resemblance to the uterine tube. "Not only are both composed of three types of cells, ciliated, non-ciliated and peg cells, but they undergo similar secretory cyclicity. . . . The close resemblance of the hydatid cysts to the tubal epithelium is further emphasized by the marked decrease in the ciliated cells and secretory activity of the postmenopausal hydatid, for similar changes occur in the oviduct following experimental or physiologic atrophy."

Fig. 6.1. Equine ovary and infundibulum of uterine tube with cystic accessory tube. Acc. No. 8736. (From Virginia Osborne, Sydney, Australia.)

Cystic Remnants of the Mesonephric Duct

Cystic remnants of the mesonephric duct are found frequently in the mesosalpinx adjacent to the uterine tube. The cysts are usually small and are seldom larger than a few millimeters in diameter. Since the cysts are so close to the uterine tube, it is sometimes difficult to determine on gross examination whether the cyst is in or adjacent to the uterine tube. In these cases, a differential diagnosis can be established by injecting India ink into the lumen of the tube. If cyst is of mesonephric origin, the ink will bypass the tube. A large cyst may compress the tube so that increased pressure is necessary for passage of the ink around the cyst.

Ectopic Adrenal Cortical Nodules

Nodules of ectopic adrenal cortical tissue are found occasionally in the mesosalpinx of the queen, bitch, cow, and mare. An intensive search would probably reveal the presence of these nodules of adrenal cortical tissue in the other species of domestic mammals. Relatively few of the nodules are large enough to be recognized readily on gross examination.

Major Congenital Anomalies

Major congenital malformations of the uterine tubes are rare in all species of domestic mammals except in cases of freemartinism in cattle and hermaphroditism in all species of domestic mammals. Congenital malformations occur much more frequently in the uterus, cervix, and vagina than in the uterine tube.

Agenesis

The uterine tubes rarely develop in bovine freemartins. Uterine tubes are present in female pseudohermaphrodites, occasionally present in true hermaphrodites, and usually missing in male pseudohermaphrodites.The only cases of agenesis of the uterine tube that I have seen occurred in intersex animals. Heinze (1964) reported a case of ovarian and tubal agenesis in a calf. He quoted Lehman to have found aplasia of the uterine tubes in sheep. Einarsson and Gustafsson (1970) reported the absence of one uterine horn as well as the uterine tube on the same side in four gilts (0.4%) in a slaughter house survey of 1000 gilts. Mack and McGlothlin (1949) recorded a case of agenesis of the right kidney associated with the absence of the right uterine horn and right uterine tube in a cat.

Segmental Aplasia

Major congenital malformations of the uterine tube occur predominantly in cattle, but even in this species such malformations are rare, even in cases of segmental aplasia of the uterus. I have found five cases of segmental aplasia of the bovine uterine tube. One cow had multiple areas of aplasia of both uterine tubes in association with bilateral segmental aplasia of the uterine horns. Another cow had segmental aplasia of the isthmus of one uterine tube. Three cows had unilateral aplasia of the infundibulum with accumulation of clear fluid in the ampulla (Fig. 6.2).

Tanabe and Almquist (1967) reported two cases of congenital malformation of the uterine tubes in a group of 180 subfertile heifers. A purebred Jersey heifer had a total absence of both infundibula. "The ampullar end of each oviduct was imperforate, resulting in a secondary hydrosalpinx of the terminal 22-mm segment of the right and 45-mm segment of the left tube." The second case was found in a purebred Holstein heifer. A 5-mm segment of the left uterine tube, approximately 28 mm from the tubouterine junction, was missing. An 18-mm portion of the tube proximal to the defect was distended with fluid to a diameter of 8 mm. The rest of the uterine tube was patent and appeared normal.

During a study of genital malformations in 2230 slaughtered cows, Settergren and Galloway (1965) found two cases of unilateral aplasia of the uterine tube. In one case it was partial and in the other complete.

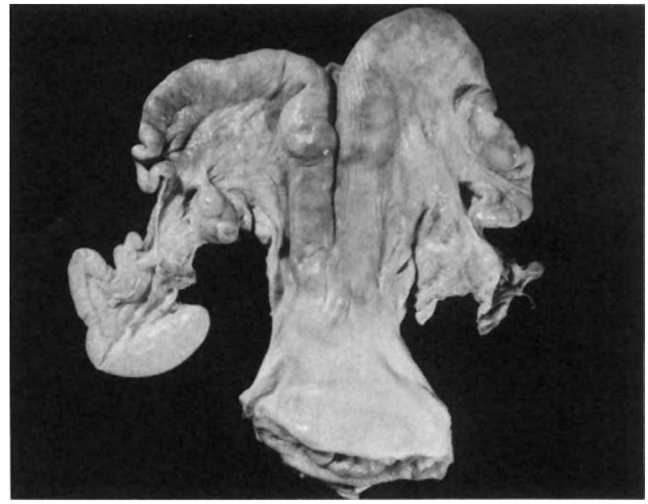

Fig. 6.2. Bovine reproductive tract. Aplasia of left infundibulum with accumulation of fluid in uterine tube. Acc. No. 16439.

I examined the reproductive tract from a 2-year-old Landrace sow with aplasia of the infundibulum of the left uterine tube. The proximal portion of the affected tube measured 30 x 16 x 5 cm and was filled with clear, watery fluid. The rest of the uterine tube appeared normal and fluid in the greatly distended area could be forced through the tube into the uterus. Einarsson and Gustafsson (1970) reported that no case of aplasia of the uterine tube was found during the postmortem examination of the genital tracts from 1000 gilts.

Sokkar and Kubba (1980) reported a case of segmental aplasia in the upper third of a uterine tube in a ewe.

Accessory Ostium

An accessory ostium is a rare malformation that I have seen only in the mare in a specimen provided by Virginia Osborne, Sydney, Australia (Fig. 6.3).

Duplication

I have seen one case of partial duplication of a uterine tube in a cow. The second tube was attached to the main tube about 7 cm from the uterotubal junction and extended distally for a distance of 5 cm. Partial duplication of the uterine tube occurs occasionally in swine.

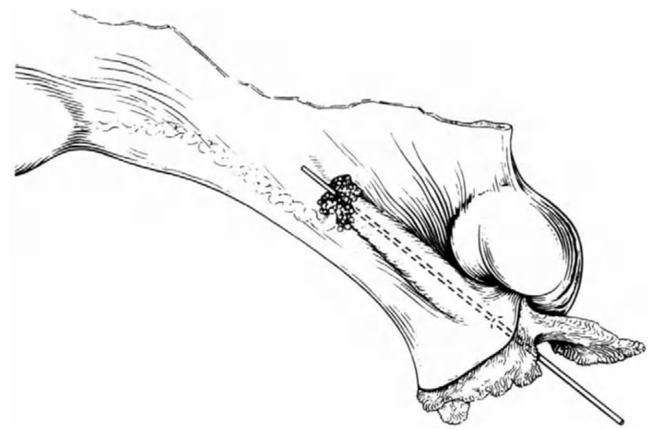

Fig. 6.3. Accessory ostium in equine uterine tube. Acc. No. 8742.

Diverticula

Küttel (1935) reported the presence of diverticula in the uterine tube of swine. The diverticula were either small cone-shaped projections or appendixlike formations a few centimeters long. The wall of the diverticula consisted of the same elements as that of the tube but certain parts of the wall were much thinner than normal.

Einarsson and Gustafsson (1970) found diverticula of the uterine tube in 14 (1.4%) of 1000 gilts: "In all cases there was communication between the relatively thin-walled diverticulum and the lumen of the oviduct." The diverticula were usually single, unilateral, and in the proximal part of the uterine tube. They suggested that the diverticula might have an adverse effect on fertility.

Salpingitis

Salpingitis and its sequelae are the most common diseases of the uterine tubes of domestic mammals. Most infectious agents enter the uterine tube via the uterus. A few diseases such as tuberculosis spread to the tube from the peritoneal cavity. Salpingitis occurs in all species of domestic mammals but appears to occur most frequently in cattle.

Cow

Carpenter *et al.* (1921) reported that 15.3 percent of 1221 cows were found, on clinical examination, to have tubal disease. They pointed out that the actual incidence of lesions in the uterine tube was probably much higher because of the inability to diagnose mild cases on clinical examination. The etiology and pathology of salpingitis in cattle have been reported by Gilman (1921), Rowson (1942a,b), Lombard *et al.* (1951), Moberg (1954), Cembrowicz (1956), Dawson (1958), and Miller and Campbell (1978).

Organisms known to cause salpinitis in the cow include streptococci, staphylococci, *Campylobacter fetus* var. *venerealis, Escherichia coli, Actinomyces pyogenes (Corynebacterium pyogenes), Brucella abortus, Mycobacterium tuberculosis, Mycoplasma* spp., and *Trichomonas fetus.* Other microbial organisms are undoubtedly involved. In most cases of bovine endometritis, which is due to a variety of organisms, the uterine tubes are usually infected. The inflammatory lesions due to microbial organisms are similar in the uterine tube and uterus and are described in Chapter 8. Many organisms, including *Campylobacter fetus* var. *venerealis* and *Trichomonas fetus,* produce relatively mild inflammatory lesions in the uterine tube. Most cows recover, leaving no residual lesions in the uterine tube. Highly pathogenic organisms, including *Actinomyces pyogenes, Brucella abortus, Mycobacterium bovis* (Fig. 6.4), streptococci, staphylococci, and *Mycoplasma bovis,* produce more severe lesions and frequently sequelae.

Hirth *et al.* (1966) inseminated 12 heifers with semen containing live *Mycoplasma bovis* organisms. *Mycoplasma* was recovered from cervicovaginal mucus for up to 8 months after insemination and from lesions observed at necropsy. "Ten of 12 heifers receiving semen containing live *Mycoplasma* required multiple insemination, and four of the 12 failed to conceive after as many as five inseminations." The four heifers that failed to conceive had chronic suppurative salpingitis, endometritis, and ovarian adhesions.

Pyosalpinx. Pyosalpinx (Fig. 6.5) is the accumulation of exudate in the uterine tube following obstruction of the lumen due to the presence of inspissated exudate, fusion of mucosal folds, or the formation of

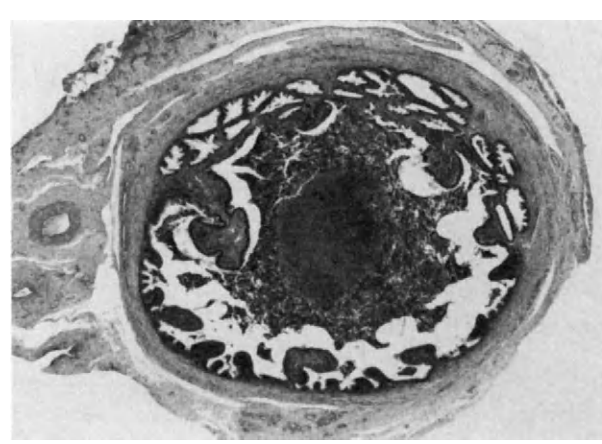

Fig. 6.4. Bovine granulomatous salpingitis due to *Mycobacterium bovis.* ×178. Acc. No. 19850.

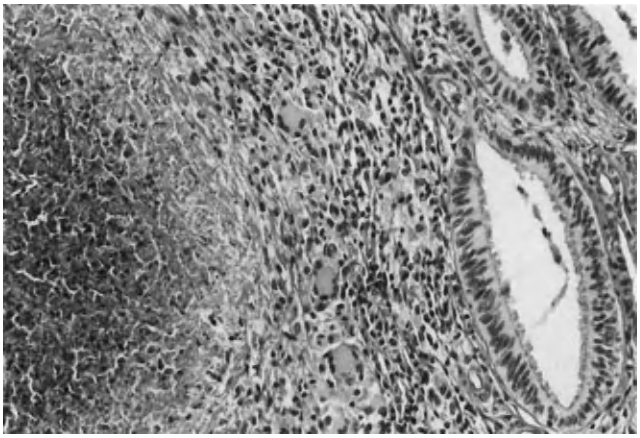

Fig. 6.5. Bovine pyosalpinx due to *Actinomyces pyogenes*. ×15. Acc. No. 5200.

granulation tissue. *Mycobacterium tuberculosis* and *Actinomyces pyogenes* are the most common causes of pyosalpinx in cattle. The entire wall of the tube is infiltrated with neutrophils, macrophages, lymphocytes, and plasma cells. Loss of epithelium on the primary, secondary, and tertiary longitudinal folds occurs and results in adhesion of the folds and cyst formation. Some of the areas of surviving epithelium may undergo squamous metaplasia. Bursal adhesions frequently accompany pyosalpinx.

Mucosal Cysts. Küttel (1935) and Lombard *et al.* (1951) described mucosal cysts in the lamina propria of the bovine uterine tube. Mucosal cysts develop following the inflammatory denuding of the epithelium on the tips of secondary and tertiary folds of the uterine tube. The areas of denuded epithelium fuse to form cysts lined by tubal epithelium (Fig. 6.6). The cysts occur predominantly in the proximal portion of the ampulla. They can be palpated as beadlike structures in the intact tube and can be observed as small cysts in the opened ampulla. Mucosal cysts do not block the uterine tube but appear to have an adverse effect on fertility. Lombard *et al.* (1951) found mucosal cysts in the uterine tube of 45 (29.2%) of 154 repeat-breeding cows. Cysts were not found in a group of virgin heifers.

Hydrosalpinx. Hydrosalpinx (Fig. 6.7) is the distention of the tubal lumen with watery fluid. It occurs in association with congenital anomalies of the uterine tubes and more frequently following acquired obstructions of the tubal lumen. Stenosis of the lumen of the uterine tube may follow severe inflammatory reactions, including pyometra, hemorrhage following enucleation of the corpus luteum, or the necrosis of tubal epithelium due to irrigation of the uterus with necrotizing solutions. In the case of pyosalpinx, the exudate is gradually replaced by a watery fluid. Blockage of the uterine tube, due to severe inflammatory lesions, occurs most frequently in the ampulla.

Adhesions. Adhesion of a portion of the fimbria of the infundibulum to the ovary and adhesions in the ovarian bursa frequently develop in association with pyosalpinx. Gilman (1921) stated that "not frequently the entire pavilion becomes adherent to the ovary, in which case there may be found a tubo-ovarian cyst or abscess." Dense adhesions frequently develop following enucleation of corpora lutea. In some cases, they are severe enough to interfere with the ability of the fimbriae of the tube to cover the ovary at the time of ovulation and therefore cause infertility. Adhesion of a portion of the fimbria of the tube to the ovary occasionally results in the accumulation of fluid in the ovarian bursa. The condition is known as a cystic ovarian bursa. In this case, the abdominal ostium of

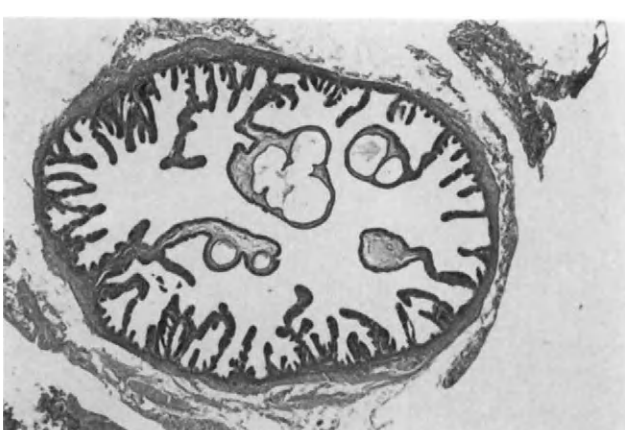

Fig. 6.6. Mucosal cysts in bovine uterine tube. ×16. Acc. No. 1087.

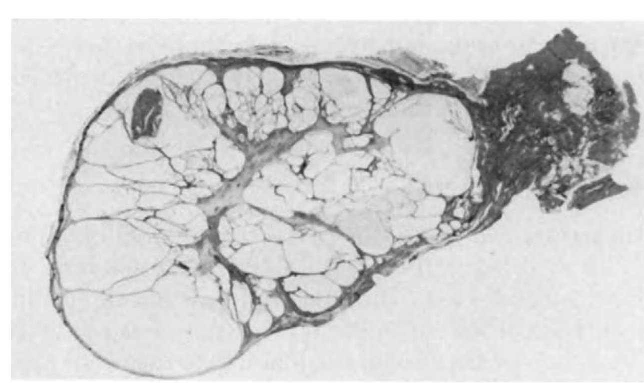

Fig. 6.7. Adhesion of uterine tube folds with cyst formation following severe salpingitis in a cow. The tubal lumen was filled with watery fluid. ×3. Acc. No. 18791.

the tube is directed toward and opens into the bursa. Thus, the flow of fluid in the tube during estrus results in the filling of the bursa with fluid. The fine adhesions that develop following ovulation (ovulation tags) do not appear to interfere with motility of the fimbriae.

Ewe

Salpingitis does not appear to occur as frequently in ewes as it does in cows. Emady *et al.* (1975) collected genital tracts from 2081 slaughtered ewes. Slight adhesions between the mesosalpinx and the surface of the ovary were present in only three specimens. These may have been ovulation tags. No gross evidence of salpingitis was noted in any of the ewes.

Adams (1975) collected 487 reproductive tracts from slaughtered ewes. Histologic examination of tissues was conducted on 194 of the reproductive tracts. Massive adhesions involving the internal genitalia were found in eight ewes. Adhesions of the mesosalpinx were seen in an additional five ewes, and four of these had hydrosalpinx. Intraepithelial cysts, similar to those described by Donaldson (1969) in the cow after prolonged treatment with oxytocin, were found in the ampulla of 116 ewes (60%) in the series of 194 cases that were examined histologically. No statistically significant association was found between intraepithelial cysts and salpingitis, endometritis, or cervical cysts. "Mild salpingitis, consisting of small accumulations of neutrophils or of lymphocytes and plasma cells with epithelial degeneration, occurred in 14 ewes (7%). In three ewes, there was a heavy infiltration of the oviductal tissue by eosinophils." Adams concluded that "the low incidence of salpingitis suggests it is of less importance as a cause of infertility in the sheep than it is in the cow."

Sokkar and Kubba (1980) examined the reproductive tracts of 110 slaughtered ewes for the presence of lesions in the uterine tubes. The following acquired lesions were found on gross and microscopic examination: adhesions between the fimbria of the uterine tube and ovary, five (4.5%) ewes; salpingitis, six (5.4%) cases; and hydrosalpinx, two (1.8%) cases.

Sow

Küttel (1935) examined 212 porcine uterine tubes collected at an abattoir. Seventy-nine of the uterine tubes had pathologic changes, of which 3.8% had salpingitis, 17% cysts, 3.3% hydrosalpinx, 1.9% mucous membrane heterotopia (adenomyosis), 10.4% perisalpingitis (adhesions), 5.2% hypoplasia, and 0.5% parasitic lesions. More pronounced and extensive squamous metaplasia was found in the porcine uterine tube than in the bovine uterine tube in association with suppurative salpingitis. Küttel referred to the presence of tubal epithelium in the muscle and under the serosa as heterotopic and indicated that it was similar to uterine adenomyosis.

Wilson *et al.* (1949) assembled 51 gilts and 28 sows that were being culled for infertility after being bred in an average of 2.8 heat periods to an average of 1.6 boars. Six breeds were represented. They were bred during their first estrus after being placed on the study. If they did not return to estrus, they were considered to be pregnant and were slaughtered. Those females that returned to estrus were rebred and slaughtered 1 and 2 days after the end of estrus. Twenty-three (45.1%) of the 51 gilts and 19 (64.3%) of the 28 sows conceived. Sixteen (58.1%) of 28 gilts and one (11.1%) of nine sows, which failed to conceive, had hydrosalpinx or pyosalpinx. Most of the cases of hydrosalpinx and pyosalpinx were bilateral with adhesions of the fimbriae to the ovaries. The etiology of the tubal lesions was not determined. Nalbandov (1952), in referring to the study by Wilson *et al.*, reported that the contents of the distended uterine tubes "were invariably bacteriologically sterile" and that "bacterial infection is probably not the causative agent of tubal abnormalities of this type." He stated that "there is some evidence that hydro- and pyosalpinges may be caused by obstruction of the oviduct by embryonal nests of the Wolffian duct system." I believe that the occlusions of the uterine tubes were induced by a previous bacterial or mycoplasmal infection that had resolved and that mesonephric duct cysts, adjacent to the uterine tube, do not cause obstruction of the tubal lumen.

Warnick *et al.* (1949) conducted a study similar to that of Wilson *et al.* with comparable results. Nineteen (43.2%) of 44 gilts and 2 (10.5%) of 19 sows had bilateral hydrosalpinx or pyosalpinx.

Wiggins *et al.* (1950) examined the reproductive tracts from 5088 slaughtered gilts and sows for the presence of gross genital abnormalities. They found tubal abnormalities (hydrosalpinx and bursitis) in 1.5% of the animals.

Mare

Vandeplassche and Henry (1977) disproved the previously accepted view that salpingitis is rare in the mare. They examined the reproductive tracts from 700 mares of different breeds and ages: "More than 40% of the infundibula had adhesions to the uterus and/or the mesovarium and/or the ovary." The incidence of adhesions was higher on the right than on the left side. The patency of the uterine tubes was determined by injecting Bouin's solution into the lumen of the tube at the proximal end and observing the uterotubal orifice for the presence of the solution.

They reported that the lumen of the ampullae in the mare was 5 to 7 mm in diameter and could hold 5 to 10 ml of solution. A higher pressure and more patience was required to force fluid through the isthmus than the ampulla. They found that nearly 100% of the uterine tubes were patent. Not a single case of hydrosalpinx was found.

Histologic examination revealed that 36 (37%) of 98 infundibula, 58 (20.8%) of 279 ampullae, and 42 (8.7%) of 483 isthmi had evidence of inflammation. The inflammatory reactions consisted, for the most part, of diffuse or focal accumulations of lymphocytes in the epithelium and lamina propria. A neutrophilic infiltrate was observed in exceptional cases. In a few cases, there was a marked infiltration of eosinophils. Salpingitis occurred more frequently on the right (60%) than on the left (40%), which was similar to the occurrence of infundibular adhesions. They stated that "it is not clear why this is so."

Henry and Vandeplassche (1981) examined the reproductive tracts of 2297 mares that were slaughtered over a period of 3 years. The mares were of various breeds, and the ages ranged from 2 to 20 years. Clinical histories were not available. Infundibular adhesions were present in 1131 (49.2%) of the animals. Unilateral adhesions were common and affected the right uterine tube most frequently. Two hundred mares had perimetritis and 157 (78.5%) of these had infundibular adhesions. No cases of total obstruction of the uterine tube were found.

"Histological examination revealed that the incidence of inflammation of the uterus was 17.2% (70% minor, 26% moderate and 4% severe) and of the utero-tubal junction was 12.2%. The incidence of inflammation of the isthmus was 3%, of the ampulla 9.4% and of the infundibulum 27%. . . . Of the cases of salpingitis examined, 84.5% were minor, 14% were moderate and 1.5% were severe. . . . Neither hydrosalpinx nor congenital abnormalities were found in the genital tracts collected in this study" (Henry and Vandeplassche, 1981).

Henry and Vandeplassche were not able to establish the cause of infundibular adhesions, which are so common in the mare. They suggested that postovulatory hemorrhage from the ovulation fossa might be responsible. This is probably the major cause of adhesions in this area.

The migration of *Strongylus edentatus* larvae causes adhesions between the fimbria of the uterine tube and the ovary and between the ovary and mesosalpinx. These adhesions are found in some sexually immature animals that have no evidence of endometritis and have not ovulated. Strongyle larvae are occasionally found around and even in the ovary. The early lesions are accompanied by an infiltration of eosinophils, which usually disappear from the site of migration by the time fibrous adhesions are well developed.

Bitch and Queen

Very little has been published concerning the pathology of the uterine tube in the bitch and queen. I have seen very few cases of salpingitis in these species. Dogs and cats with cystic hyperplasia–pyometra complex usually do not have salpingitis. I have observed suppurative endometritis and bilateral salpingitis in young Beagle bitches that had been treated with estrogen for a prolonged period of time. The lumen of the uterine tube was distended with neutrophils. A dense infiltration of neutrophils occurred in the tunica propria and serosa. Exudate was present in the ovarian bursa and focal area of suppurative inflammation were present on the ovarian surface. Focal areas of squamous metaplasia were present in the endometrium and in the mucosa of the uterine tube.

Acquired Cysts

Intraepithelial Cysts

Donaldson (1969) reported the presence of intraepithelial cysts (Fig. 6.8) in the uterine tube and endometrium of cows that had received daily injections of oxytocin for 30 to 68 days. The cysts were up to 7 μm in diameter and were found in the infundibulum and ampulla but not in the isthmus. The histogenesis of the cysts was not determined. I have seen similar cysts, but not as extensive, in the epithelium of the fimbria and to a lesser extent in the ampulla of cows on Days 9 through 30 postpartum.

Cystic Epithelial Recesses

Andersen and Simpson (1973) stated that "the most common abnormality of the fimbriae and proximal portion of the oviduct in ageing Beagles was found to

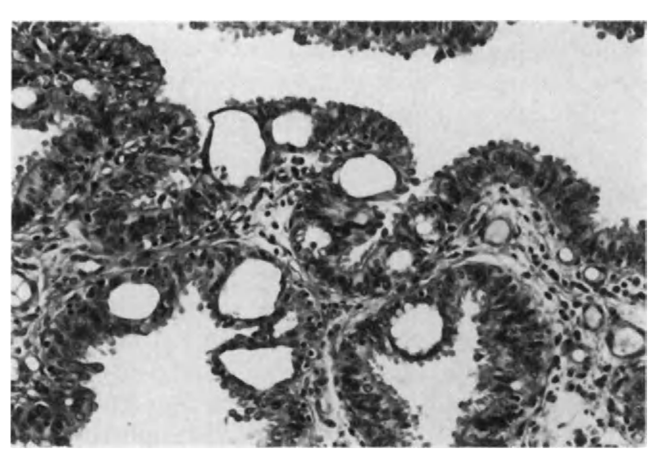

Fig. 6.8. Intraepithelial cysts in bovine uterine tube. Fourteen days postpartum. ×178. Acc. No. 10896.

be cysts." The cysts ranged in size from 0.1 to 1.0 mm and were located in the depths of the mucosal folds. Similar mucosal cysts occur in the uterine tube of the cat. These mucosal cysts of the uterine tube in the cat and dog arise from epithelial-lined recesses of the tubal lumen in contrast to mucosal cysts in cattle, which are secondary to salpingitis and fusion of mucosal folds.

Mucosal cysts are described under the sequelae of salpingitis.

Cystic ovarian bursae and tubo-ovarian cysts are described in Chapter 4, dealing with cysts in and around the ovary.

Squamous Metaplasia

The porcine uterine tube is more prone to develop squamous metaplasia, in association with salpingitis, than the uterine tubes of other species of domestic mammals (Küttel, 1935).

Palludan (1966) reported squamous metaplasia of the uterine tubes in gilts on vitamin A-deficient diets. The lesions started as "subepithelial metaplasia, and rather characteristically, they commenced in numerous foci from which the individual foci spread." The lesions were present throughout the uterine tube. It was emphasized that "no infectious changes in connection with the metaplasia in the oviducts were observed." Squamous metaplasia of the endometrium was extremely rare. It was seen in only one gilt that had multiple small foci of endometrial metaplasia.

The mycotoxin zearalenone (F-2) produced by a species of *Fusarium* causes squamous metaplasia of the uterine tubes, uterus, cervix, vagina, and mammary glands of swine (Chang *et al.*, 1979).

Sokkar and Kubba (1980) reported the occurrence of squamous metaplasia of the uterine tube in association with chronic salpingitis in the ewe. I have seen similar lesions in the cow.

Adenomyosis

Küttel (1935) described adenomyosis of the porcine uterine tube and referred to the condition as mucous membrane heterotopia. I have seen extension of the epithelium into the muscularis and to the subserosa of the uterine tube in the bitch and queen.

A comparable condition in women has been called salpingitis isthmica nodosa, diverticulosis, and adenomyosis. Some consider it to be a postinflammatory lesion and others believe it is induced by hormonal stimulation. Wheeler (1982) stated that "evidence for a noninflammatory adenomyosis-like origin is more convincing. Moderate or large numbers of endometrial-like stroma cells accompany the diverticula in over half of the cases. . . . Unilateral tubal involvement is often accompanied by uterine adenomyosis on the same side." Newbold *et al.* (1984) reported that the lesions can be induced in mice by administering diethylstilbestrol dissolved in corn oil on Days 1 to 5 of neonatal life.

Neoplasms

Neoplasia of the uterine tube is extremely rare in domestic mammals. Andersen and Simpson (1973) reported "a presumably radiation-induced adenoma of the fimbriae" of the uterine tube in a Beagle bitch. I have seen two adenomas and one adenocarcinoma of the uterine tube in dogs. One adenoma occurred in the infundibulum of the uterine tube in a 7½-year-old Labrador Retriever bitch that was on a long-term radiation experiment. The other adenoma occurred in an 8½-year-old Boxer bitch. A 12-cm mass was attached to the hilar region of the left ovary. Portions of this neoplasm were provided by Dr. M. G. Maxie of Ontario Veterinary College, Guelph. The tumor consisted of abundant smooth muscle and fibrous tissue arranged in interwoven bundles. The surface of the mass consisted of papillary proliferations of connective tissue covered by epithelial cells varying from low cuboidal to columnar. Cilia were present on the tall cells. Tubular structures extended from the surface of the neoplasm into the underlying connective tissue. A few small areas of squamous metaplasia were scattered throughout the tumor. This neoplasm was diagnosed as an adenomyoma of the uterine tube.

An adenocarcinoma was found in a 12-year-old Shepherd dog of mixed breeding. The bitch was pre-

Fig. 6.9. Ventral view of canine reproductive tract. Carcinoma of fimbria in left uterine tube. Acc. No. 8790.

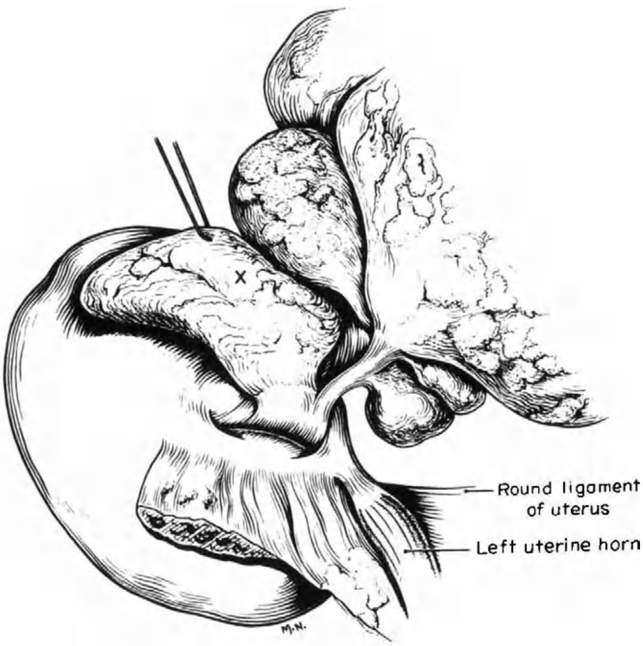

Fig. 6.10. Carcinoma of fimbria in canine uterine tube. The neoplasm has been lifted from the opening to the ovarian bursa. Acc. No. 8790.

Fig. 6.12. Adenoma of the fimbria of an equine uterine tube. Acc. No. 8739.

sented with inappetence, lethargy, and a greatly distended abdomen. She had never been bred and had regular estrous cycles until 9 years of age; she remained anestrus for the next 3 years. Laparotomy revealed a large mass, which appeared to originate from the left ovary, and there was about 600 ml of serosanguinous fluid in the peritoneal cavity. Tumor implants were noted on the abdominal wall. The bitch recovered from an ovariohysterectomy but a long-term follow-up of the case was not obtained. The reproductive tract was submitted by Dr. F. B. Tierney, New York, New York. A shaggy lobulated

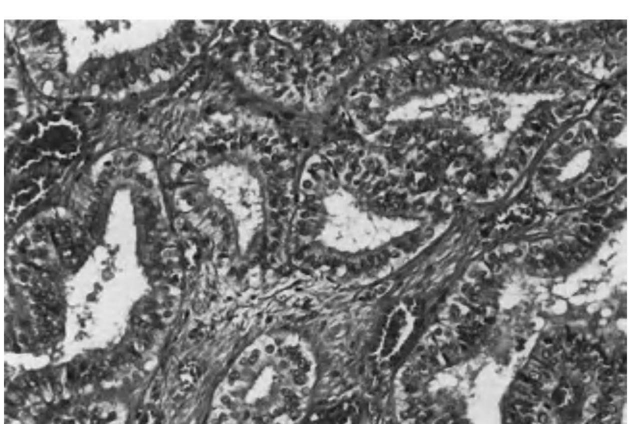

Fig. 6.11. Carcinoma of canine uterine tube. × 178. Acc. No. 8790.

mass of tissue measuring 16 x 22 x 25 cm protruded from the opening of the right ovarian bursa (Figs. 6.9 and 6.10). A 10 x 9 x 6-cm neoplastic mass was confined by the bursa. The left ovary was not involved. The neoplasm closely resembled mucosa of the infundibulum (Fig. 6.11). Mitotic figures were scarce. It was classified as adenocarcinoma on the basis of implants in the peritoneal cavity. Minoccheri and Meluzzi (1979) reported an adenoma of a canine uterine tube.

Dr. Virginia Osborne, Sydney, Australia, submitted a papillary adenoma of the infundibulum from a mare. It was an abattoir specimen, and a clinical history was not available. The neoplasm consisted of a large shaggy mass of tissue extending from the infundibulum (Fig. 6.12). Histologically, the neoplasm closely resembled the mucosa of the normal infundibulum.

Carcinomas of the uterine tube are uncommon in women. Hu *et al.* (1950) reported "twelve primary carcinomas of the Fallopian tube out of 3,878 primary malignant lesions of the female genital tract in the 90,611 admissions from 1903 to 1948, an incidence of 0.31 percent of primary malignant tumors."

I have seen unilateral lipomas of the mesosalpinx in two aged bitches. Benesch (1952) described and illustrated a case of torsion of a lipoma involving the left mesosalpinx of a 4-year-old Dachshund bitch.

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Chapter 7
The Uterus: Anatomy

Cow
Ewe and Doe (Goat)
Sow
Mare
Bitch
Queen
Bibliography

The uterus of domestic mammals consists of a cervix, a uterine body (corpus), and two uterine horns (cornua). The cervix is discussed in Chapter 12. The body of the uterus extends from the internal cervical os to the bifurcation of the uterine horns. The uterine horns diverge from the cranial end of the uterine body. The uterine horns are fairly straight in the bitch, queen, and mare, and are coiled in the cow, ewe, doe, and sow.

The uterus consists of three layers: endometrium (mucosa), myometrium (muscularis), and perimetrium (serosa). The endometrium is lined by columnar or cuboidal cells. Simple branched tubular glands extend from the uterine lumen to the muscularis. Caruncles, which are nonglandular portions of the endometrium, are present in ruminants. The caruncles consist of highly cellular connective tissue. The myometrium consists of a thick inner circular and an outer longitudinal layer of smooth muscle. A vascular zone consisting of large arteries, veins, and lymphatics is located between the muscle layers. The serosa, the layer of longitudinal muscle, and the stratum vascular are continuous with the broad ligaments that suspend the uterus.

The broad ligaments contain a considerable amount of smooth muscle. The mesometrium is the part of the broad ligament that terminates on the horn and body of the uterus. A secondary fold of the broad ligament arises from the lateral surface of the mesometrium. The round ligament of the uterus is located in the free edge of this fold, which begins near the tip of the uterine horn and blends with the peritoneum over the deep inguinal ring.

Cow

The uterine body of the cow is very short with a range in length of 2 to 4 cm. The uterine horns are coiled and in nonpregnant cattle are from 20 to 45 cm long, depending on age and parity (Perkins *et al.*, 1954). The tips of the uterine horns are S-shaped. Cranial to the uterine body, the uterine horns are united for a considerable distance by a common peritoneal covering, connective tissue, and external layer of muscle, which gives the false impression that the uterine body is relatively long. Dorsal and ventral intercornual ligaments are located at the point of divergence of the uterine horns. A shallow recess is present between the intercornual ligaments.

Each uterine horn contains approximately 50 caruncles arranged in four longitudinal rows. Caruncles are present at birth. The caruncles are slightly elevated, dome-shaped protuberances consisting of densely cellular connective tissue that is devoid of endometrial glands. Melanophores are present in the caruncles of Jersey cows.

Uterine glands are absent at birth in normal calves (Fig. 7.1). Kennedy *et al.* (1957) reported the presence of uterine glands in a Guernsey fetus that had undergone prolonged gestation as a result of adenohypophyseal aplasia. The surface epithelium of normal calves gradually invades the lamina propria to form glands during postnatal life (Fig. 7.2). The surface epithelium of the endometrium is pseudostratified columnar and that of the glands is columnar. The uterine glands are branched, coiled, tubular structures that extend to the myometrium. The ducts of the glands become straight as they pass through the compact endometrial stroma beneath the surface epithelium. The uterine glands are evenly distributed between the caruncles and underlie the caruncles.

The endometrial stroma consists of a relatively narrow superficial zone, the zona compacta, and a much broader deep zone, the stratum spongiosa. The zona compacta consists of densely cellular fibrous tissue containing numerous capillaries. The fibroblasts

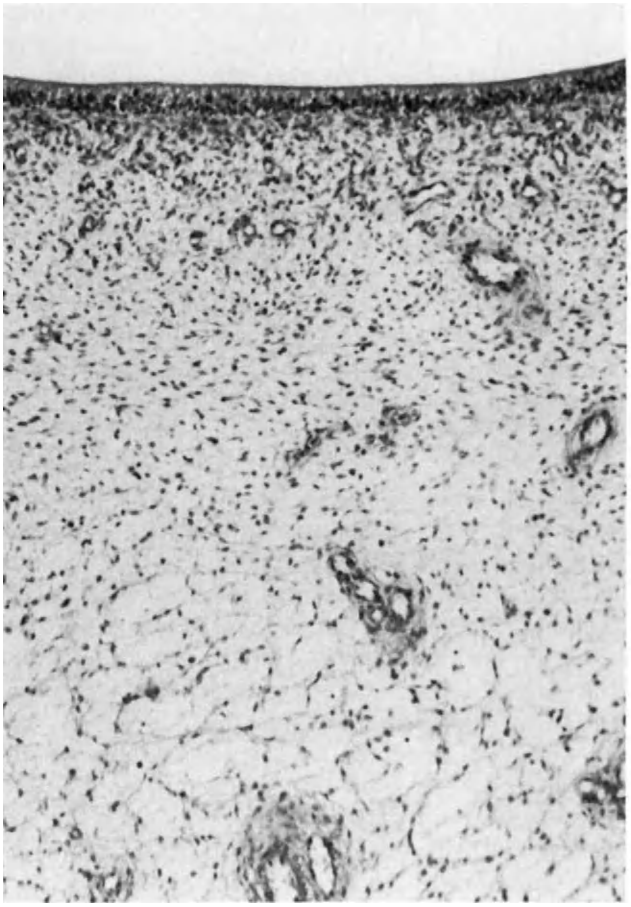

Fig. 7.1. Endometrium from a 2 1/2-hour-old normal calf. Endometrial glands not developed. ×122. Acc. No. 7371.

Fig. 7.2. Endometrium from a 29-day-old normal calf. Glands growing in from the surface epithelium. ×122. Acc. No. 7355.

in this area have large, pale-staining nuclei. The stratum spongiosum consists of loose connective tissue with many more fibrillar elements than the stratum compactum. The fibroblasts have smaller, dark-staining nuclei and the collagen bundles form trabeculae between the endometrial glands.

The histologic changes in the endometrium of the cow during the estrous cycle have been described by Cole (1930), Asdell *et al.* (1949), Weeth and Herman (1952), Skjerven (1956a,b), Vollmerhaus (1957), and van den Hoek (1959). The histologic changes in the endometrium of the cow during the estrous cycle are not as dramatic as those occurring in other species, especially primates.

In referring to the cow, Weeth and Herman (1952) commented that "morphological and histochemical changes which occur in the oviduct and uterus during the estrous cycle are minor." The estrous cycle of the cow is divided into four stages: proestrus, estrus, metestrus, and diestrus. The only marked gross changes of the reproductive organs are those associated with estrus and subsequent metrorrhagia (uterine hemorrhage), which occurs 24 to 72 hours after the onset of estrus. During estrus there is edema of the tunica propria of the endometrium and the glands are relatively straight. The edema subsides and the glands become more coiled and complex as the level of progesterone produced by the developing corpus luteum increases. The epithelial cells of the glands reach their maximum height at about the eighth day following ovulation. The surface epithelial cells are relatively tall during estrus, cuboidal at 2 days postestrus, and reach a maximum height at Days 9 to 12 of the cycle (Hansel and McEntee, 1977).

Metestrous uterine bleeding (metrorrhagia) occurs in about 50% of cows (Hansel and Asdell, 1952) and 80 to 90% of heifers (Trimberger, 1941; Weber *et al.*, 1948a). Macroscopic evidence of blood discharged from the vulva by 24 to 72 hours after estrus varies from a slightly red tinged mucus to a copious flow of blood. Weber *et al.* (1948b) reported that "microscopic bleeding into the uterus by diapedesis began just prior to ovulation. In the caruncular areas the epithelium remained intact during the massive hemorrhage on the second day postestrus. In the intercaruncular areas, many sites of epithelial rupture and direct capillary hemorrhage into the uterine lumen were seen."

Weber *et al.* (1948b) reported the occurrence of "cytoplasmic disintegration and nuclear pyknosis" of the uterine gland epithelium. Their Fig. 1, illustrating these changes, is characteristic of the alterations seen in association with postmortem autolysis secondary to improper fixation. They stated that "incisions were made in the uterine horns at intervals to facilitate rapid fixation." The entire genital tract was then placed in fixative. To avoid postmortem autolysis the uterine horns must be opened and small segments placed in fixative.

Skjerven (1956b) and van den Hoek (1959) investigated the cyclic changes in the populations of inflammatory cells in the bovine endometrium. Neutrophils are normal constituents of the superficial layers of the endometrium during estrus when they may occur in large numbers. Neutrophils are rare or absent during the progestational phase of the cycle. The increase in the number of neutrophils during estrus is associated with increased resistance of the uterus to infection (Black *et al.*, 1953; Rowsen *et al.*, 1953). Eosinophils may be present in large numbers in the endometrium without apparent relationship to fertility. A definite cyclic variation has not been demonstrated. According to van den Hoek, lymphocytes are more numerous in the subepithelial zone of the endometrium than any other cell type, and they are more evenly distributed. No cyclic variations are evident. The occurrence of dense, multifocal, lymphocytic infiltrates is abnormal. A few plasma cells may be present in the superficial layers of the endometrium at all stages of the estrous cycle.

Likar and Likar (1964) reported that the bovine endometrium contained only a few mast cells during metestrus and that they were located mainly beneath the lining epithelium. The number of mast cells increased slowly during diestrus and the staining became more intense. "In prooestrus the number of mast cells increased beneath the lining epithelia and also around uterine glands. In late prooestrus or early oestrus, it appeared that the accumulation of mast cells reached a peak and the degranulation became more noticeable. After or during oestrus a sudden diminution of mast cell numbers was observed, particularly in the endometrial stroma."

Ewe and Doe (Goat)

The uterus of the ewe and doe has anatomic features similar to those of the cow. Cole and Miller (1935) studied the histologic changes in the endometrium of the ewe during the estrous cycle. Considerable edema of the tunica propria of the endometrium occurs during proestrus and estrus. "At this time the necks of the uterine glands are composed of high columnar cells, whereas at the base of the glands the epithelium is low columnar. During metoestrum the epithelium at the base of the glands is converted to the high columnar type; these glands show evidence of growth; and there is increased coiling of the glands, their greatest complexity being observed at the end of the first week following oestrus." The free surface of the uterine mucosa becomes somewhat folded at the seventh day of metestrum. Cole and Miller stated that "the uteri of most ewes autopsied in mid-anoestrum are easily distinguished from those autopsied during the sexual season. The uterine glands and all other portions of the uterine mucosa recede to a point not seen at any other reproductive phase of the mature ewe." During anestrus the surface and glandular epithelium are low cuboidal. The number of glands is small, and the diameter of the uterus is reduced.

The caruncles of sheep are frequently pigmented from the presence of melanoblasts (Grant, 1933). The pigmentation is especially prominent in ewes with heavily pigmented skin but according to Grant, "heavy pigmentation of the uterine mucosa is found in breeds of sheep such as the Border Leicester and Cheviot, in which skin pigmentation has to a large extent been eliminated by selective breeding." The melanin pigment is confined to caruncles in virgin ewes. During pregnancy the pigment becomes dispersed in intercaruncular tissue (Fig. 7.3). According to Grant some melanoblasts are destroyed by the fetal trophoblast during pregnancy. Emady *et al.* (1975) stated that in the ewe "there was a greater degree of pigmentation in nulliparous and primiparous than pluriparous specimens and a reduction in the amount of pigmentation with advancing pregnancy." They also reported that "of the 2081 specimens examined, melanin was completely absent, on macroscopic examination, from only four specimens." In two ewes the pigment was located in only one uterine horn. Pigmentation of the caruncles also occurs in some goats (Lyngset, 1968).

Sow

In the sow the body of the uterus is 3 to 5 cm long and the uterine horns are extremely long and flexous. Rigby (1968) reported that "the mean length of the uterine horn was 64.6 cm during the postweaning oestrus and 81.5 cm during the subsequent oestrus periods." The uterine horns are thick and edematous during estrus, and they become thinner and double in length as edema subsides after the end of estrus. Rigby reported that the mean length of the uterine horn, in a group of experimental sows, was 70.3 cm

Fig. 7.3. Ovine uterus with melanin pigment in caruncles and scattering of pigment in intercaruncular tissue of right uterine horn. Acc. No. 20513.

during estrus and 134.3 cm during diestrus. The length of the uterine horn, in abattoir specimens, was 82.3 cm in estrous sows and 171.3 cm in diestrus sows. "The length of the uterine horn was similar throughout oestrus, and lengthening of the horns did not start until 7 to 10 hours after the end of oestrus (80 to 83 hours after the onset of oestrus). . . . The Fallopian tube did not change in length after the end of oestrus" (Rigby, 1968).

Endometrial glands are not present in the newborn pig (Hadek and Getty, 1959). According to Erices and Schnurrbusch (1979), the endometrial glands begin to develop from the superficial epithelium in the second week of life and reach the basal part of the endometrium in the fourth week. They reported that "both the number of uteroglandular sections per visual field and the glandular surface over the whole area of the endometrium, as recorded from cross-section specimens, increased strongly over the first three months of age, followed by less marked change. . . . Stagnation in uterus development and growth was observed at the age of over 180 days."

Schnurrbusch and Erices (1979) described the histologic changes in the endometrium of gilts during the first three estrous cycles. They stated that "during one cycle, significant variation was recorded for the height of surface epithelium (maximum: metoestrus), the percentual amount of glands in the total area (maximum: metoestrus to dioestrus I), and the number of glandular sections in one visual field (maximum: dioestrus I). The first sexual cycles, hence, are characterized by continued uterus growth and more stabilization of uterus function. Gilts, therefore, should not be used for breeding until the second oestrus has taken place."

Mare

A detailed anatomic description of the uterus of the mare has been presented by Ginther (1979). The uterine body is much larger than that of other species of domestic mammals and is approximately the same length as the uterine horns. Warszawsky *et al.* (1972) reported that the mean dimensions of the uterine horns in saddle mares were 14.8 cm long × 3.4 cm wide for the left side and 15.2 cm long × 3.4 cm wide for the right side. The mean weight of the uterine body and uterine horns was 696 g.

The endometrium has prominent longitudinal folds consisting of a gland-free core of connective tissue covered by endometrium. The longitudinal folds of the endometrium continue into the cervix. The epithelial lining cells of the endometrium are columnar, and pseudostratification occurs during estrus. The lamina propria consists of the stratum compactum, which is about 1 mm thick, and the stratum spongiosum, which is a loose arrangement of connective tissue with considerable interstitial fluid. The uterine glands are branched, tubular, and greatly coiled. The glands may have 10 or more primary branches and fewer secondary branches. The glands are lined by simple columnar epithelium.

Kenney (1978) described the histologic changes in the endometrium of the mare during the estrous cycle. During proestrus the luminal epithelium is columnar and of low to moderate height. It varies from simple columnar to pseudostratified. The luminal epithelium reaches its greatest height during early estrus and diminishes to low columnar in late estrus in some mares. Although neutrophils marginate in capillaries and venules in the zona compacta during estrus, large numbers do not leave the vessels. Estrual edema decreases the gland density per unit area. Metestrus, which is the transitory period between estrus and diestrus, is not identified easily by histologic examination. The gland density increases during diestrus as a result of diminished stromal edema and increased tortuosity of the glands. The endometrium becomes atrophic during anestrus. According to Kenney, seasonal atrophy "is often noticeable as early as July, long before cessation of behavioral and ovarian signs of anestrus." The anestrus endometrium is characterized by a cuboidal luminal epithelium "with increased basophilia of the cytoplasm, a non-edematous lamina propria, and relatively straight, non-tortuous glands, with low columnar epithelium."

Endometrial cups are round to oval, gray, elevated areas of endometrium with central concavities that are present in the gravid uterine horn in the mare between 37 and 150 days of gestation. Their presence is associated with the production of pregnant mare's serum gonadotrophin (PMSG). According to Ginther (1979), "there is general agreement that PMSG is first detectable on approximately Days 37 to 42 in individual mares, rises rapidly to peak at Days 55 to 65, and then declines slowly to very low or non-detectable levels by Days 120 to 150." Clegg *et al.* (1954) reported that "the endometrial cups invariably develop in that portion of the endometrium in apposition to the chorion in the region where the allantoic vessels fan out over the allantochorion from the umbilical vessels."

The endometrial cup consists of densely packed, large polyhedral cells with abundant pale eosinophilic cytoplasm. Allen and Moor (1972) and Allen *et al.* (1973) demonstrated that the large polyhedral cells of the endometrial cups originate from the chorionic girdle portion of the trophoblast. Many of the cells are binucleated. Endometrial glands are present throughout the cup. Numerous lymphocytes and a few plasma cells and eosinophils are present around the periphery of the endometrial cup at 50 days of gestation. The endometrial cups gradually degenerate from the 60th to the 150th day of pregnancy when the necrotic cups are rejected from the endometrium.

Bitch

The uterine body of the bitch is short and the uterine horns are very long, of uniform diameter in the normal nonpregnant state, and relatively straight. The endometrium may be arranged in four to five low, longitudinal folds. Transverse dark bands, consisting of pigment-laden macrophages, demarcate implantation sites from previous pregnancies.

The endometrium of the bitch consists of three zones: the zone of crypts, the intermediate zone, and the basal zone (Barrau *et al.*, 1975). The crypt zone has numerous short, epithelial-lined recesses of the uterine lumen. A crypt zone is not present in other domestic mammals. The intermediate zone is composed predominantly of connective tissue. The glands in the intermediate zone continue into the basal zone, where they branch, coil, and terminate.

The cyclic changes in the endometrium of the bitch have been described by Evans and Cole (1931), Mulligan (1942), Anderson and Wooten (1959), Fitch (1963), Sokolowski *et al.* (1973), and Barrau *et al.* (1975). During anestrus the epithelial lining of all three zones is low columnar or cuboidal and the glandular lumina contain abundant debris. The uterus is rather flattened during anestrus and becomes rounded transversely during proestrus and estrus. Marked edema of the lamina propria occurs by the first day of proestrus, as well as marked hypertrophy and some hyperplasia of the glandular cells. According to Barrau *et al.*, "Proestrus is characterized principally by the differentiation of glandular epithelium into large mucus-secreting cells." Extensive extravasation of red blood cells occurs into the superficial part of the endometrium. Macrophages accumulate in the areas of extravasation to phagocytize the red blood cells. Barrau *et al.* reported that "By the fourth day of estrus, however, a second and even more dramatic burst of growth within the endometrium is initiated. The height of the glands increases, the mitotic index increases from near 0 to 1.5, and the glandular epithelial cells hypertrophy. By the end of estrus, the basal glands exhibit a significant increase in coiling and the crypts appear to be appreciably elongated and coiled." The uterine glands grow rapidly at the onset of metestrus, and the basal glands become highly coiled and branched. Uterine growth is nearly completed by the sixth day of metestrus. The uterus has the gross appearance of being coiled when under the influence of progesterone. This is due to the bulging of the myometrium between subserosal blood vessels. Regressive changes in the endometrium occur after the 16th to 20th day of metestrus when the levels of plasma progesterone begin to fall. The surface epithelial cells develop a very finely vacuolated cytoplasm during the regressive phase of metestrus. The endometrium becomes thinner in the region of the crypts and intermediate zone, and debris accumulates in the glands in late metestrus. Macrophages are abundant in the stroma during the regressive phase of metestrus. The endometrium returns to the anestrus state by the end of metestrus.

Queen

The gross anatomy of the uterus of the queen is similar to that of the bitch. Dawson (1950) described the morphologic changes in the endometrium of the cat from the anestrus condition until the time of implantation and the changes resulting in pseudopregnancy, which are associated with an infertile mating or cervical stimulation. The endometrial glands are straight, narrow, and relatively short in the anestrous queen. The surface and glandular epithelia are low cuboidal, and there are no cells in mitosis. During proestrus and estrus, the glands dilate but remain straight. The surface and glandular epithelia increase in height, and mitotic figures are present. In the early luteal phase of the cycle, the glands enlarge and become tortuous. Abundant glycogen accumulates during early pregnancy in the basal part of the epithelial cells and displaces the nuclei apically, the glycogen deposits are rapidly reduced during the second week after mating, and the surface epithelium forms narrow papillary folds. The glycogen deposits are depleted by the time of implantation. Similar changes occur during pseudopregnancy with the exception that there is necrosis of the papillary surface tissue, neutrophilic infiltration of the adjacent endometrium, and sloughing of the necrotic tissue during the termination of pseudopregnancy.

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Chapter 8

The Uterus: Congenital Anomalies

Minor Congenital Anomalies
- Mesonephric Duct Remnants

Major Congenital Anomalies
- Aplasia of the Uterus
- Uterus Unicornis
- Segmental Aplasia of the Uterus
- Uterus Bicorpor Bicollis (Uterus Didelphys)
- Transverse Mucosal Occlusions and Folds
- Duplication of Uterine Horns
- Agenesis of Uterine Glands
- Multiple Defects in the Reproductive Tract

Bibliography

Minor Congenital Anomalies

Mesonephric Duct Remnants

Remnants of the mesonephric duct occur frequently in the uterus of domestic mammals and are located either in the mesometrium adjacent to the myometrium or in the myometrium. Usually they are found only by chance when sections of uterus include the mesometrium. The remnants of the mesonephric duct are lined by cuboidal epithelium, surrounded by smooth muscle, and tend to become cystic in aged animals. Cystic remnants are seen most frequently in aged bitches, and multiple cysts are not uncommon. The histology of mesonephric duct remnants in domestic mammals has received very little attention but has been studied in detail in the human female (Gilbert and Sheorey, 1941; Gardner *et al.*, 1948; Huffman, 1951; Bransilver *et al.*, 1973).

Major Congenital Anomalies

Major congenital malformations of the uterus are uncommon in domestic mammals except in swine, freemartins, hermaphrodites, and certain inbred lines of cattle including White Shorthorns. Goethals (1951) found that 18 (1.8%) of 1000 reproductive tracts from swine slaughtered in Belgium had major malformations of the uterus. In a slaughterhouse survey conducted in Denmark, Teige (1957) found 84 (0.98%) of the reproductive tracts from 9250 gilts and 5 (1.05%) of 476 sows had major uterine malformations. A slaughterhouse survey in Sweden revealed the presence of 12 (1.2%) major uterine anomalies in a series of 1000 gilts (Einarsson and Gustafsson, 1970).

Zemjanis *et al.* (1961) diagnosed only three (0.01%) cases of uterus unicornis and nine (0.04%) cases of "white heifer disease" during the clinical examination of 20,913 cows in Minnesota and Wisconsin. Lagerlöf and Boyd (1953) found uterine anomalies in only 4 (0.06%) of 6286 reproductive tracts from slaughtered Swedish Highland cows.

Segmental aplasia of the tubular genitalia in cows is commonly referred to as "white heifer disease." Spriggs (1946) stated that "Descriptions in the literature are a little confusing, and it is clear that a number of abnormalities have been included under the heading of 'white heifer disease'." It was pointed out that "No single lesion is characteristic of 'white heifer disease' although some are more common than others." According to Spriggs, the most common features in order of frequency in eight animals were "(a) An imperforate hymen or a hymen persisting to a varying degree, often with the vulvo-vagina terminating near this point. (b) A cystic distention of one or both uterine horns, the uterine body being present in a very rudimentary form. (c) A complete absence of cervix and anterior vagina. (d) Prominence of the Wolffian or mesonephric rudiments. (e) Presence of longitudinal submucous channels in the vagina. (f) Aplasia of one uterine horn." The term *white heifer disease* was introduced at the turn of the century because of the relatively frequent occurrence of the condition in White Shorthorn cattle. It is unfortunate that the term has been adopted so widely because it is neither specific nor descriptive. The occurrence of segmental aplasia of the reproductive tract is not always associated with a lack of pigmentation of the hair coat. It is preferable to diagnose the condition according to the type and location of the defect or defects. Different types of segmental aplasia of the reproductive organs occur in different breeds and strains of cattle and the modes of inheritance differ.

The condition in White Shorthorns "is considered to be inherited in a polygenic pattern" (Leipold, 1978). Rendel (1952) reported the incidence of "white heifer disease" in a large herd of Shorthorns: "The 7 bulls tested sired 9 affected white heifers out of 23, 4 affected roans out of 115 and 1 affected red out of 94." The author did not examine the animals and pointed out that "some cases classified as white heifer disease may have been some other genital abnormality very similar to, but with a different origin from, white heifer disease."

Fincher and Williams (1926) reported arrested development of the paramesonephric ducts, resulting in sterility, in 12 of the 23 daughters in a family of Holstein-Friesians produced by sire–daughter matings. Gregory *et al.* (1945) concluded that "this apparently is a clear-cut case of a single recessive autosomal gene conditioning female fertility." Bennett *et al.* (1973) commented that "The same ratio would be expected if the defective gene had been sex-linked and carried on the X chromosome."

Bennett *et al.* (1973) reported that "When a Holstein-Friesian bull, a known carrier of white heifer disease, was mated to his female offspring, 12 abnormal and 37 normal heifer calves were produced." They concluded that "The genes for white heifer disease are: (1) not sex-linked, (2) are autosomal recessive, (3) very likely separate for left and right horn abnormality and (4) linked with genes for left and right on the same chromosome."

Nordlund (1956) reported a 3% incidence of malformation of the reproductive tract in Swedish Friesian heifers that had been sired by the same artificial insemination sire. The affected heifers were detected because of the impossibility of inseminating them. "Usually it was impossible to introduce the insemination catheter more than 6 to 7 cm. Rectal examination usually revealed a fluctuating distention of the vagina, often the size of a man's head. . . . The animals showed normal oestrus and did not vary in type or colour from normal heifers." Postmortem examination revealed that the vagina had failed to develop, to varying degrees, in 8 of 12 heifers. The caudal part of the vagina was imperforate in 7 of the heifers and only the vestibule of the vagina was present in the 8th animal. The vagina was distended greatly with viscous mucus discolored by blood. Malformations were present in the cervix and/or uterus in 10 of the 12 cases. The ovaries, uterine tubes, and vulva were normal in all the heifers. The malformations of the reproductive tract in the Swedish Friesian heifers are similar to those in White Shorthorns.

Aplasia of the Uterus

Aplasia of the entire uterus is extremely rare except in a few freemartins and some hermaphrodites. Most of the cases of uterine aplasia involve segments of one or both uterine horns or an entire uterine horn with the exception of a small portion of the affected horn near the ipsilateral uterine tube. In a few cases, one entire uterine horn and ipsolateral uterine tube may be absent (Einarsson and Gustafsson, 1970). Aplasia of the uterus may occur alone or in association with varied degrees of aplasia of the cervix and vagina.

Uterus Unicornis

Uterus unicornis refers to the congenital absence of one uterine horn. Usually a small, cystic cranial portion of horn is present. Cows, ewes, and sows with uterus unicornis may become pregnant, but fertility is usually reduced.

Uterus unicornis is the predominant congenital malformation that has been reported in the ovine uterus. Gustafsson and Holmberg (1966) found one case of uterus unicornis, affecting the right uterine horn, in a series of 502 slaughtered ewes. It was the only congenital uterine defect in the series. Ansari (1978) found five cases of uterus unicornis during the examination of the reproductive tracts from 3590 slaughtered ewes. The left uterine horn was affected in four animals. McCracken and Caldwell (1969) reported the congenital absence of the left uterine horn in a ewe that had not exhibited estrus for 58 days, whereas the rest of the flock was cycling normally. Hunter (1970) described the reproductive organs of two ewes in which the left uterine horn and oviduct were congenitally absent, but in which estrous cyclic activity was normal. O'Shea *et al.* (1974) reported normal estrous cycles in five ewes in which the left uterine horn was congenitally absent. They reported that "In all these ewes, the blood vessels supplying the left ovary were essentially normal, and large uterine veins drained into the left utero-ovarian vein. Normal cyclical activity in these circumstances is consistent with a mechanism of luteolysis involving countercurrent transfer of prostaglandin F_2 in the uterine and ovarian vessels." The presence of uterus unicornis on the left side in 12 of 14 reported cases in sheep appears to be more than a chance occurrence.

Sheppard (1951) reported 21 cases of uterus unicornis in cats and found a frequency of one per 1000 animals. The ovary and uterine tube were present on the affected side in all cases. No mention was made of renal involvement. It is quite possible that the kidneys were not examined. Robinson (1965) described a case of uterus unicornis in a cat with ipsilateral renal agenesis and referred to similar individual cases reported by Radasch (1908) and Mack and McGlothlin (1949). Both ovaries were present in three queens. The associated absence of a uterine horn and the ipsilateral kidney can be explained by the fact that the uterus and part of the kidney develop from the mesonephros. The ovaries have a separate embryologic origin, the gonadal ridges.

Höfliger (1971) conducted a literature survey on the occurrence of unilateral agenesis of the kidney in domestic mammals. Ninety cases were reported in swine, 39 in cattle, 5 in sheep, 2 in goats, 12 in horses, 46 in dogs, and 21 in cats. A "remarkably frequent occurrence" of the defects was found in Beagles. "Apart from rudiments of the accompanying ureter, the defective side shows deformities in the male and female genital tracts, the latter particularly in cats and rabbits, as well as anomalies in other organs."

Williams and Fincher (1938) recorded a case of uterus unicornis and unilateral renal agenesis in a term equine fetus with failure of abdominal closure. Both ovaries were present.

Segmental Aplasia of the Uterus

In cases of segmental aplasia of the uterus, the body of the uterus may be absent, a segment or most of one or both uterine horns may be missing (Figs. 8.1 and 8.2), or multiple areas of one or both uterine horns may be aplastic. Animals with unilateral aplasia of the uterus may conceive, but their fertile life is usually reduced (Fig. 8.3). Roberts (1950) described three cases of aplasia of the distal part of the right uterine horn in three Guernsey cows that had calved several times. The blind uterine horn contained soft calculi in each case and, in two of the cows, it was diagnosed clinically as a mummified fetus. In the third case, "The feeling elicited from palpation of this cystic apex was very similar to that felt on palpating a macerated fetus."

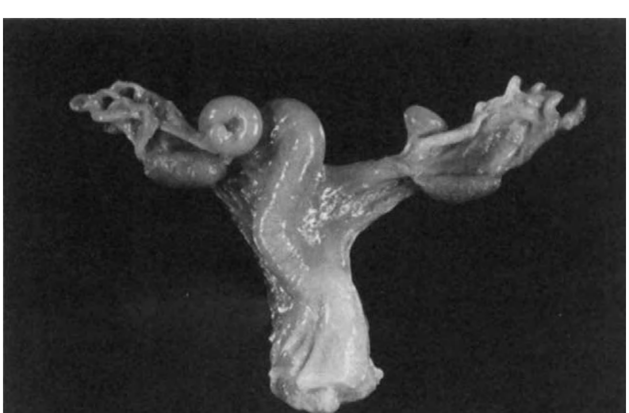

Fig. 8.1. Aplasia of right uterine horn from a newborn Holstein calf. Acc. No. 20261.

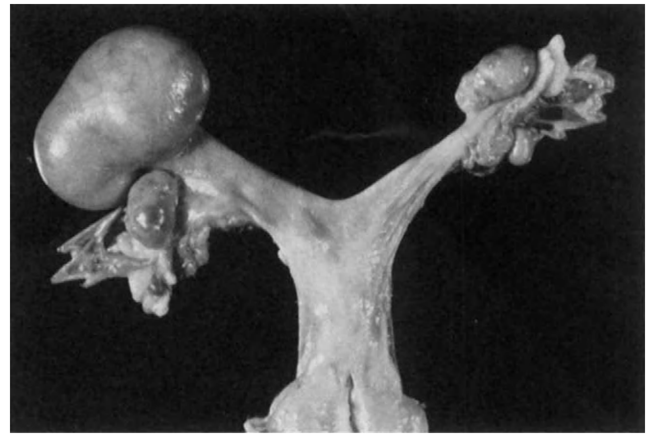

Fig. 8.2. Aplasia of both uterine horns in a 1 1/2-year-old Holstein heifer. Accumulation of fluid in persistent cranial part of left horn. Vagina was aplastic. Acc. No. 18794.

I examined the reproductive tracts from two Ayrshire heifers that were the offspring of sire–daughter matings. All the heifers from these matings were reported to be sterile. The two reproductive tracts, which I examined, had bilateral, symmetrical blind segments in the proximal third and in the distal portions of both uterine horns (Fig. 8.4). The body of the uterus was moderately dilated with mucus and estrual debris. The cervix and vagina were patent.

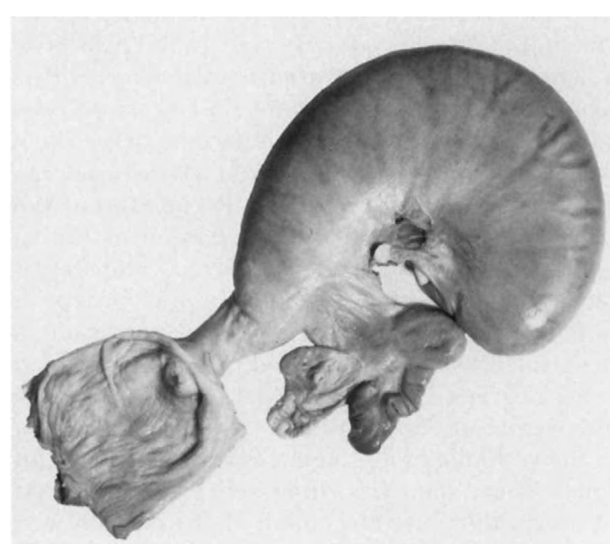

Fig. 8.3. Aplasia of right uterine horn from a 3-year-old Guernsey heifer with an 18-cm fetus in the left uterine horn. Acc. No. 989.

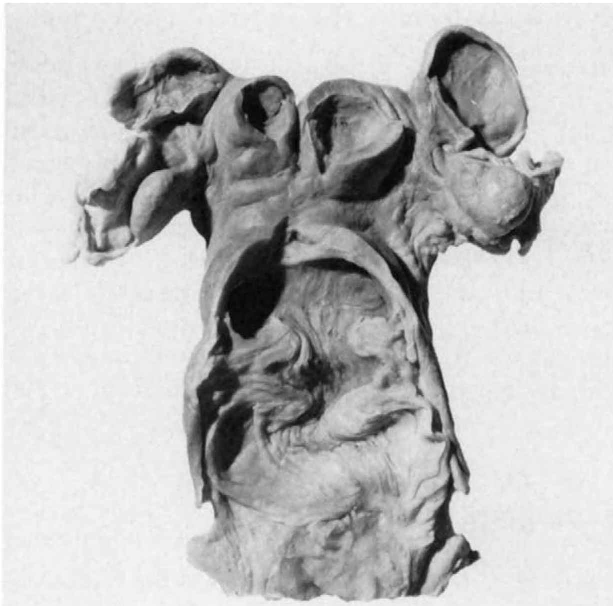

Fig. 8.4. Bilateral segmental aplasia of uterine horns from an Ayrshire heifer. Acc. No. 2116.

Teige (1957) examined the genital organs from 9250 gilts and 476 sows in slaughterhouses in Denmark: "In the routine killing at the slaughterhouses, the genital tract is cut across sometimes immediately caudal to the cervix. Therefore, in the first 7,473 animals examined (7,108 gilts and 365 sows), inspection of vagina was exceptional. For the remaining 2,253 (2,142 gilts and 111 sows), the whole of the genital canal was examined." Aplasia of both uterine tubes and uterine horns as well as aplasia of the uterine body, vagina, and ovaries was found in 12 cases. The vulva appeared to be normal. Uterus unicornis was diagnosed in 16 animals (14 gilts and 2 sows), and segmented aplasia of one or both uterine horns was found in 36 cases (34 gilts and 2 sows). "In six cases of uterus unicornis, the tube and ovary on the side concerned were lacking. In the other ten cases, the tube and ovary were present but the horn was completely lacking. Residue of the apex of the missing uterine horn in the form of a minor cyst, seen in most cases of uterus unicornis in cows, was found in no case" (Teige, 1957). Partial duplication of one uterine horn was found in 11 animals. Aplasia of the vagina, cervix, uterine body, and portions of the uterine horns was observed in 10 animals. Four gilts had uterus didelphys. The two cervices were somewhat thinner and longer than normal.

I have seen two cases of bilateral aplasia of the proximal two-thirds the uterine horns in dogs. I have seen one case of aplasia of the distal portion of the uterine body in a cat (Fig. 8.5). The uterine horns were evenly distended with fluid.

Fig. 8.5. Aplasia of feline uterine body with fluid accumulation in uterine lumen. Acc. No. 1578.

Uterus Bicorpor Bicollis (Uterus Didelphys)

The term uterus bicorpor bicollis designates a uterus consisting of a complete double cervix and a divided uterine body. Tanabe and Almquist (1967) stated that the term uterus didelphys when applied to cattle "is limited, technically, in its accuracy and suitability, in view of (i) the definitions of uterus didelphys—'double uterus due to failure of the ducts of Müller to unite' (Stedman, 1982) and "either of two distinct uteri occurring side by side in the same individual" (Dorland, 1988); (ii) the subtotal duplication of the uterus in the cases reported; and (iii) the possible occurrence, though remote, of a true double uterus with a complete duplication of all its components."

Transverse Mucosal Occlusions and Folds

Peterson *et al.* (1966) reported the occurrence in infertile heifers of "segmental aplasia of the uterine mucosa, characterized by the presence of a partial or complete wall across the uterine lumen, the myometrium being normally developed. This defect was found in the anterior horns of four heifers. In two of them, there was a partial occlusion of one horn by a permanent annular fold of endometrium, which reduced the uterine lumen to about half its normal diameter. In the other two heifers, the lumen of each horn was completely occluded at one to three places." An abnormal amount of fluid did not accumulate in the occluded segments. I have seen ventral mucosal folds in the cranial portion of the uterus in Holstein cattle.

Duplication of Uterine Horns

Duplication of a portion of a uterine horn appears to occur most frequently in swine (Teige, 1957). Dhindsa and Dziuk (1967) reported partial doubling of the uterine horns in 5 of approximately 500 gilts. They stated that "three of the gilts were pregnant, the re-

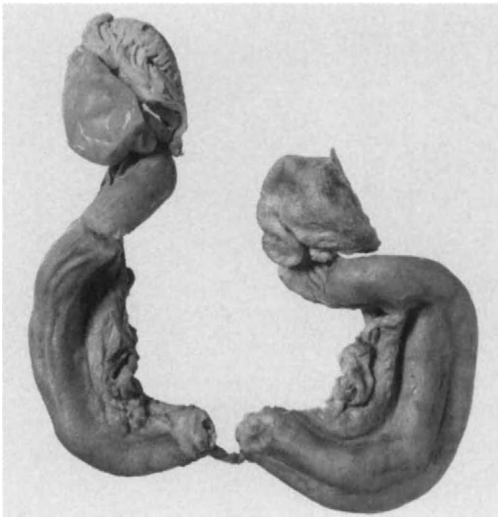

Fig. 8.6. Duplication of the right uterine horn from a cat. Acc. No. 83.

maining two had blind horns which may have prevented the continuance of pregnancy." They speculated that the anomaly "may be genetically influenced." Two of the affected gilts were half-sisters. I have seen the defect in the sow, cow, and queen (Fig. 8.6).

Agenesis of Uterine Glands

I have seen two cases of agenesis of uterine glands in Holstein-Friesian heifers. Caruncles, endometrial stroma, and surface epithelium were present. The affected heifers came into estrus, ovulated, and developed corpora lutea that persisted because of an apparent lack of a luteolytic factor in the endometrium.

Fig. 8.7. Bovine reproductive tract with multiple malformations. Arrow points to opening between uterine horns. Acc. No. 5427.

Multiple Defects in the Reproductive Tract

I have seen one very unusual case of multiple defects in the reproductive tract of a Holstein-Friesian heifer. The uterus apparently twisted during early embryonic development, prior to the formation of the vagina, so that the left uterine horn crossed over the right horn and each opened separately into the vagina (Fig. 8.7). The left cervix, which was located on the right side, had two cervical rings, and the right cervix had only one poorly developed ring. The ovary that was located on the right side was enclosed within a membrane, and the uterine tube opened into the cystic cavity.

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Chapter 9

The Uterus: Normal Postpartum Involution

Cow

Ewe

Doe (Goat)

Sow

Mare

Bitch
  Placental Sites
  Interplacental Site Endometrium

Queen
  Placental Sites
  Interplacental Site Endometrium

Bibliography

To recognize and evaluate pathologic alterations in the postpartum uterus, it is first essential to know the gross and microscopic changes that occur during normal involution. Uterine involution in domestic mammals has been investigated in all species but most extensively in the cow and the ewe. Most studies have been concerned with the time of return of the uterus to its approximate pregravid size, but the uterus is not prepared for the maintenance of normal pregnancy at this stage. Additional time is required for the establishment of the normal physiologic functions necessary for conception and maintenance of pregnancy. Involution occurs most rapidly in the mare and sow and least rapidly in the bitch.

Cow

Morrow *et al.* (1969a), Garcia (1982), and Leslie (1983) reviewed the literature on postpartum involution of the bovine uterus. Garcia stated that "the postpartum period in the cow starts with parturition and lasts until uterine involution is completed and the animal has resumed regular oestrous cycles with normal oestrous behavior."

The interval from parturition to complete uterine involution is significantly longer in pluriparous than in primiparous cows (Buch *et al.*, 1955; Morrow *et al.*, 1966). Marion *et al.* (1968) reported that the "average intervals from parturition to complete involution for primiparous and pluriparous cows were 34.0 and 40.6 days, respectively, a highly significant ($p < 0.01$) difference." Garcia and Larsson (1982) conducted clinical examinations and plasma progesterone assays of dairy cows during 183 postpartum periods. They stated that "the present data indicate the duration of the post partum period to be 40–50 days. After this period uterine involution is completed and the cow has regular cyclic ovarian activity."

I have examined the reproductive organs from 15 Holstein-Friesian heifers that had calved for the first time. All had delivered normal calves and appeared to be disease free. They were slaughtered from 2 through 30 days postpartum. The uteri were cultured for bacteria and fungi. The ovaries and uterine tubes were separated from the rest of the reproductive tract and the broad ligaments were removed adjacent to the junction with the uterine horns. The uterine content was removed and measured. The uterine horns were separated from the cervix and each horn was measured and weighed. Tissue sections were prepared from the cranial, middle, and caudal portions of each horn. The weights of the uterine horns, characteristics of the lochia, and culture results are presented in Table 9.1. The uterus, minus the cervix, weighed 7175 g in one cow at Day 2 postpartum and 3567 g in another cow at Day 4. The average uterine weight was 793 g at Days 12 to 15 and 509 g at Day 30. The previously gravid horn weighed about 100 g more than the nongravid horn at Day 30, which is in agreement with the report by Wagner and Hansel (1969).

Gier and Marion (1968) examined the reproductive tracts from 57 clinically normal cows at Day 1 through Day 60 following parturition. Each uterus was trimmed of excessive fat and separated from the

Table 9.1
Postpartum Uterine Involution in the Cow

Day	Accession Number	Uterine Weight (g) Gravid	Nongravid	Total	Cervical Weight	Uterine Content	Culture Results
2	9295	5050	2215	7265	600	710 ml, thin, bright red fluid	*E. coli* *C. perfringens*
4	9245	3180	387	3567	647	165 ml, dark red fluid	Sterile
9	9410	1121	483	1604	534	1000 ml, thick, brown-red fluid with tan particles	*S. bovis*
10	9227	944	391	1335	303	500 ml, dark red-brown, mucoid material	Sterile
12	9216	523	270	793	272	25 ml, thick brown fluid with sandlike particles	*E. coli*
13	6760	554	204	758	292	—[a]	Sterile
15	9194	539	290	829	238	Small amount of clear mucus	Sterile
16	6768	424	246	670	256	—	Sterile
17	6769	337	161	498	224	—	Sterile
22	6702	245	176	421	267	—	Sterile
30	7358	316	211	527	145	Small amount of clear thin mucus	Sterile
30	7410	253	164	417	217	No content	Sterile
30	7556	346	208	554	180	No content	Sterile
30	7610	345	223	568	140	No content	Sterile
30	7615	298	180	478	143	No content	Sterile

[a]Not recorded.

vagina by cutting the tract 20 mm caudal to the external os. The uterus was weighed, measured, and photographed. Placental remnants and uterine fluids, if any, were removed and weighed. They reported that "The weight of the average uterus decreased from 9.0 kg at parturition to 1.0 kg at 30 days and to 0.75 kg at 50 days." The weight of uterine fluid ranged from 800 to 2000 g from Day 1 through Day 8 postpartum with the largest amount on Day 6. The uteri contained 125 to 750 g of fluid from Days 10 through 16.

The volume of uterine content in my cases varied from 165 to 1000 ml during the first 9 days postpartum. Very little fluid was present after Day 12. The color of the uterine fluid changed from bright red to dark brown as the interval from parturition to slaughter increased. Tan particles of necrotic caruncular tissue were present in the fluid during Days 6 and 9.

Rasbech (1950) conducted clinical examinations of postpartum heifers and cows. He reported that "A few primiparae discharge almost no lochia, but absorb practically the entire uterine contents. Older multiparae discharge from 800 to 2,000 ml lochia." The average lochial discharge in heifers was 500 ml.

Elliott *et al.* (1968) cultured uteri for bacteria from 106 postpartum cows. Luminal washings and endometrial tissue were inoculated into six different media and incubated at 37°C under atmospheric conditions, increased carbon dioxide, and strict anaerobic conditions. "Bacterial recoveries were made from 93 percent of the uteri from cows three to 15 days, 78 percent of those between 16 and 30 days, 50 percent between 31 and 45 days and only nine percent of those between 45 and 60 days." Thirty-three different species of bacteria were isolated from 66 to 106 uteri: "*Staphylococcus epidermidis* was isolated from 15 uteri; *Pseudomonas* sp., 12 times; *Corynebacterium bovis* seven times; and *Streptococcus faecalis* and *Micrococcus* sp. four times each. . . . Thirty-six recoveries were made from tissue inoculum only, two were recovered from luminal flushings only and 28 from both tissue and flushings." It appears to be necessary to use tissue inoculum as well as uterine content for determining uterine infections in postpartum cows.

Rasbech (1950) reported that "Infection with *Corynebacterium pyogenes* in pure culture in puerperal cows is the most frequent (28.3 percent). This infection is accompanied by considerable macroscopic changes in the lochial discharge, which becomes more purulent towards the end of the involution period, being whitish or yellowish white." Pure cultures of *Escherichia coli* were found in 26.7%, pure cultures of staphylococci in 16.7%, and mixed bacterial infections in 25% of the cows.

In the postpartum heifers which I examined, *E. coli, Streptococcus bovis,* and *Clostridium perfringens* were isolated from the uteri of animals slaughtered on Days 2, 9, and 12 postpartum. The uteri were bacteriologically sterile in heifers slaughtered on Days 4, 10, and 13 through 30. According to Arthur (1975), "the negative pressure which is present in the genital tract immediately after expulsion of a fetus induces an in-rush of air and this often causes contamination and later colonization of the uterus by organisms which normally populate the vestibule of the particular species."

Bretzlaff and Ott (1983) determined the prevalence of uterine infection in pastured beef cows during the first 2 weeks after calving. They sampled "uterine contents using modified Teigland swabs with a double-glove technique." The prevalence of positive cultures was 9 of 26 (35%), which "was less than reported for normally calving postpartum dairy cows subjected to the same method of uterine sampling." Nine of 12 samples (75%) collected from dairy cows within 5 days of calving yielded bacterial isolates. These cows calved in continuously occupied maternity stalls that were undoubtedly contaminated.

The gross changes in the normal postpartum bovine uterus are most prominent in the caruncles. The caruncular tissue above the vascular stalk undergoes necrosis and fragmentation and is sloughed into the uterine lumen. By Day 2 postpartum, irregular, wedge-shaped, red areas are present in the luminal half of the caruncle. By Day 4, the caruncles are dark red and soft. The dark discoloration extends to the vascular stalk, which is white. By Days 9 to 12, all the necrotic caruncular material has sloughed from the surface of the stalk leaving a granular surface with a few small hemorrhagic foci. It continues to have a granular, nonglistening surface until it is covered by the in-growth of adjacent surface epithelium. The surface epithelium in the intercaruncular areas of the endometrium remains intact throughout the postpartum period, giving the surface of the intercaruncular tissue a glistening appearance. If the epithelium is denuded as a result of endometritis, the surface appears granular and nonglistening. The endometrium is light to dark brown from the presence of hemosiderin-laden macrophages. The surface of the caruncles begins to glisten by Day 15 because of the regeneration of the surface epithelium. By Day 30, the caruncles appear to be normal on gross examination. The endometrium is still brown because of the presence of hemosiderin.

The sequential histologic changes during postpartum involution of the bovine uterus have been reported by Rasbech (1950), Gier and Marion (1968), Wagner and Hansel (1969), and Archbald *et al.* (1972). The following description of the histologic changes are based on material that I have examined. All the specimens were from clinically normal heifers. Fifteen previously mentioned specimens were obtained following slaughter and three were collected by incising a portion of the uterine wall through a flank incision. The latter specimens were provided by Dr. Katherine Bretzlaff of the University of Illinois. The histologic descriptions are based on examination of the previously gravid uterine horn.

Day 2—Postmortem Specimen (Acc. No. 9295)

Hemorrhagic infarcts (Fig. 9.1), associated with degenerative and proliferative vascular lesions, were present in many of the caruncles on Day 2 postpartum. The lesions occurred in arteries as they passed through the thick zone of collagenous connective tissue on the superficial part of the vascular stalk of the caruncle. Early vascular lesions consisted of hydropic degeneration of the cells in the intima and adjacent media. Some of the nuclei of affected cells were enlarged and others pyknotic. Intimal proliferation of loosely arranged spindle-shaped cells with abundant, pale blue cytoplasm narrowed the arterial lumen and apparently caused blockage of the vessels in the fibrous tissue septa of the caruncle. Multifocal colonies of large, gram-negative rods were present in the infarcts. *Escherichia coli* and *C. perfringens* were isolated from the uterus. Most of the crypts in noninfarcted areas of the caruncle were filled with necrotic epithe-

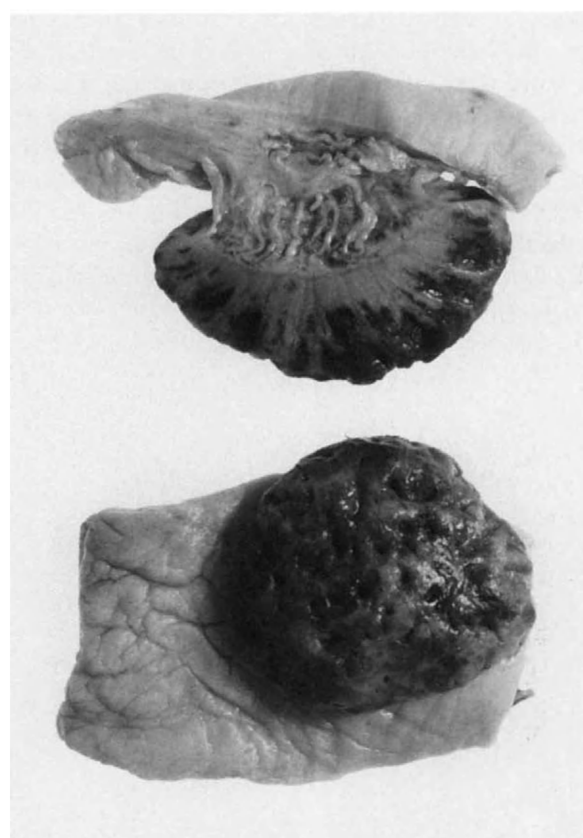

Fig. 9.1. Intact and incised caruncles from a cow 2 days postpartum. The wedge-shaped dark areas in the cut specimen are foci of infarction. Acc. No. 9295.

lial cells. Viable maternal epithelium was present in only a few areas. The depths of a few crypts contained viable trophoblastic cells and fetal placental mesenchyme.

The surface epithelium was intact throughout the uterus. It consisted of pseudostratified columnar cells, some of which contained basal vacuoles. The zona compacta was thick and contained numerous eosinophils and a few neutrophils. Dense focal accumulations of these cells were present below the surface epithelium and many were migrating through the epithelium.

The zona spongiosa was edematous and contained widely dilated lymphatics. The endometrial glands were dilated, lined by low columnar epithelium, and surrounded by a zone of collagenous connective tissue. Numerous large, spherical cells with abundant, coarsely granular, blue-gray, cytoplasmic bodies were located in the basal portion of the epithelium. The nuclei of normal-appearing cells were adjacent to the lumen. Archbald *et al.* (1972) reported that these degenerative changes occur in the glandular uterine epithelium of the prepartum cow.

Day 4—Postmortem Specimen (Acc. No. 9245)

Infarction of the caruncles involved most of the tissue above the vascular stalk (Fig. 9.2). The connective tissue septa were spared and had an increased amount of collagen fibers. The vascular lesions in the stalk were more advanced than at Day 2. In addition to the arterial lesions, there was degeneration of veins in and below the zone of dense fibrous tissue. Wavy bands of hyaline material were present in the venous walls, and loosely arranged fibrous tissue had proliferated adjacent to the endothelium. The walls of the veins were not uniformly involved. Neutrophils, eosinophils, macrophages, and a few multinucleated giant cells were present in the periphery of the necrotic tissue and in the zone of fibroblasts. Small mononuclear cells were evenly dispersed among the fibroblasts, and there was neoformation of small blood vessels. A few small islands of viable chorionic tissue were present in some caruncles. Bacteria were not isolated from the uterus nor were bacteria found in the infarcted tissue.

Fig. 9.2. Intact and incised caruncles from a cow 4 days postpartum. All the caruncular material is necrotic down to the stalk. Acc. No. 9245.

The surface epithelium in intercaruncular areas was intact and consisted of cuboidal to columnar cells that were not pseudostratified as at Day 2. Some of the epithelial cells had basal vacuoles containing hyaline droplets. Collagen fibers were increased in the zona compacta, which contained a few small lymphocytic foci. The collagen fibers surrounded blood vessels and were dispensed throughout the zona compacta. Polymorphonuclear leukocytes were not evident.

Less edema of the zona spongiosa was present than on Day 2 and the lymphatics were partially collapsed. The endometrial glands were moderately dilated and surrounded by prominent collagen fibers. The glandular epithelium was low columnar and contained a few mitotic figures. Large cells with coarse, blue-brown, cytoplasmic granules were present in the basal part of the epithelium. Macrophages with similar pigment were present in the lumina of endometrial glands and in the connective tissue surrounding some of the glands.

Day 5—Biopsy Specimen (Acc. No. 19611)

Numerous interstitial cells with foamy cytoplasm (foam cells) and multinucleated giant cells surrounded dark blue cellular debris in the caruncles. The small arteries in the collagenous zone of the stalk had thick muscular walls and very small lumina. The mesenchymal tissue had proliferated and resembled the normal stroma of the nongravid caruncle. This proliferation occurred beneath the dense connective tissue zone of the caruncle and appeared to be an early stage of regeneration. A portion of fetal placenta was present on the edge of some caruncles. Pyknosis and karyorrhexis of the chorionic mesenchyme had occurred, but the trophoblastic cells were viable.

Cuboidal to columnar epithelium covered all the intercaruncular endometrium. Large apical vacuoles were present in many of the epithelial cells. Abundant collagen was present in the zona compacta. Most of the endometrial glands had small lumina and were lined by low columnar epithelial cells with relatively little cytoplasm. The epithelial cells were taller in the glands near the zona compacta. The lymphatics were not prominent and abundant collagen was present in the depth of the endometrium. Relatively few inflammatory cells were evident in the endometrium.

Day 7—Biopsy Specimens (Acc. Nos. 19613 and 19661)

Granulation tissue with small islands of necrotic material covered the caruncular stalk. Large areas of hemorrhage surrounded the areas of necrosis. Many of the mesenchymal cells had heavily vacuolated cytoplasm. There was pyknosis and karyorrhexis of the cells in the intima and media of arteries and thrombosis of veins. The amount of collagenous connective tissue covering the caruncular stalk was reduced, and it had disappeared adjacent to large blood vessels. Nonorganized thrombi were present in veins in the caruncular stalk. Epithelium covered most of the stalk.

The intercaruncular tissue was covered by columnar epithelium. A few neutrophils were present in the zona compacta and in the surface epithelium. Less collagen was present in the zona compacta than on Days 4 and 5. Most of the glands in the depth of the endometrium had small lumina containing a few macrophages and were lined by low columnar epithelium containing a few pyknotic cells. Some of the basal glands were lined by flattened to columnar epithelium and were surrounded by abundant collagenous connective tissue. A few glands contained brightly eosinophilic, granular material and pyknotic nuclei.

Day 9—Postmortem Specimen (Acc. No. 9410)

The caruncular stalks were short and broad. Surface epithelium extended for a short distance up the edge of the caruncles. The major portion of the caruncular surface was covered by granulation tissue and exudate. A few large areas of hemorrhage were present in the superficial part of some of the caruncles. In a few areas, the intima of arteries contained abundant, loosely arranged fibrous tissue.

Columnar epithelium covered the intercaruncular endometrium. Small, multifocal lymphocytic foci and a few neutrophils and eosinophils were present in the stratum compactum. A pure culture of *Strep. bovis* was isolated from the uterus. Moderate-sized islands of collagen fibers were dispersed throughout the stratum compactum.

The endometrium was comparatively narrow and collagen fibers were abundant, especially in the basal area. The glands were lined by columnar epithelium. A few necrotic cells and macrophages were present in the lumina. Cells with pigment-containing cytoplasm were present in the basal part of the epithelium, and pigmented macrophages were present in the connective tissue surrounding the glands. Neutrophils and eosinophils surrounded occasional glands.

Day 10—Postmortem Specimen (Acc. No. 9227)

Bacterial cultures of the uterus were sterile. Epithelium had not regrown over caruncles in the previously gravid uterine horn (Fig. 9.3). The histology of the uterus was similar to the uterus on Day 9, with the exception that there were no pockets of exudate in the caruncles. Lymphocytic foci were present in the intercaruncular endometrium.

Day 12—Postmortem Specimen (Acc. No. 9216)

Escherichia coli was isolated from the uterus following slaughter. Only a small amount of lochia was present in the uterine lumen (Fig. 9.4). Epithelium was growing in from the sides of the caruncle, but the major

Fig. 9.3. Ten-day postpartum bovine uterus with denuded epithelium in the caruncles of the right uterine horn. Acc. No. 9227.

Fig. 9.4. Twelve-day postpartum bovine uterus with small amount of lochia in the uterine lumen. Acc. No. 9216.

portion of the caruncular surface was denuded. Less granulation tissue was present than on Day 9, and there was a marked proliferation of normal-appearing caruncular stroma. A few necrotic blood vessels protruded through the surface of the caruncles. Organizing thrombi were present in some of the vessels in the stalk. Large lymphocytic foci were present in the stroma.

The epithelium covering the intercaruncular endometrium was low to tall columnar. Large, oval to spherical basal cells with pale brown cytoplasmic granules were present in the epithelium. Many neutrophils and lymphocytes were migrating through the surface epithelium. Large perivascular lymphocytic foci were present in the stratum compactum.

A few endometrial glands adjacent to caruncles were widely dilated, lined by cuboidal to flattened epithelium, and surrounded by a wide zone of collagen fibers. It appeared that these glands were obstructed during involution of the caruncles. The rest of the endometrial glands had small lumina and were lined by columnar epithelial cells. Pigmented cells were present in the basal portion of the epithelium and macrophages containing dark brown cytoplasmic pigment granules were located in the surrounding stroma.

Day 13—Postmortem Specimen (Acc. No. 6760)

The caruncles were partially covered by epithelium. Prominent lymphocytic foci were present in the caruncular stroma, and there were a few small lymphocytic foci in the stratum compactum of the intercaruncular endometrium. No bacteria were recovered from the uterus.

Days 15, 16, and 17—Postmortem Specimens (Acc. Nos. 9194, 6768, and 6769)

A small amount of clear mucus was present in the uterine lumen on Day 15 and the surface of the caruncles was beginning to glisten (Fig. 9.5). Bacteria were not isolated from the uteri on Days 15, 16, and 17. The edges of the caruncles were covered by epithelium, but the central portions were denuded. Large lymphocytic foci were present in the superficial caruncular stroma. Many of the arteries in the caruncular stalks had light blue, lacy, intimal fibrous tissue.

The amount of collagen in the intercaruncular en-

Fig. 9.5. Fifteen-day postpartum bovine uterus that is devoid of lochia. Acc. No. 9194.

dometrium had decreased. Some of the glands adjacent to caruncles were dilated and surrounded by a wide zone of collagen fibers. Perivascular and periglandular accumulations of lymphocytes and eosinophils were present in a few areas of the stratum spongiosa. The stratum compactum was relatively free of inflammatory cells.

Day 22—Postmortem Specimen (Acc. No. 6702)

Some of the caruncles were covered by epithelium, but others had denuded centers. Prominent lymphocytic foci were present in the caruncles and in the zona compacta of the intercaruncular tissue. A large amount of pale blue, lacy, fibrous tissue was present in the intima of the caruncular arteries. This lesion extended along the vessels into the myometrium. Cystic glands with flattened epithelium and periglandular fibrosis were present adjacent to and underlying some of the caruncles.

Day 30—Postmortem Specimens (Acc. Nos. 7358, 7410, 7556, 7610, and 7615)

These cases were selected at random from a large series of clinically normal heifers slaughtered 30 days after parturition. The uteri were bacteriologically sterile in all cases.

All the caruncles were covered by columnar epithelium. The vascular lesions were similar to those present in the Day 22 uterus. Numerous macrophages with pale brown, cytoplasmic pigment granules were present in the caruncular stroma and in the zona compacta of the intercaruncular endometrium. Lymphocytic foci were present in the caruncular stroma and in the stratum compactum in three of the five heifers.

More investigations need to be conducted on the morphology and microbiology of the postpartum uterus of the cow. The literature reports concerning the histology of the postpartum bovine uterus are rather sketchy. I have described the histologic changes in the endometrium in a limited number of bovine uteri at Days 2 through 30 postpartum. The infected uteri of heifers slaughtered on Days 2 through 12 revealed histologic differences from those that were bacteriologically sterile. The infected uteri had colonies of bacteria in necrotic caruncular tissue, dense neutrophilic infiltrates, and large perivascular lymphocytic foci in the glandular portion of the endometrium. The popular belief that all postpartum bovine uteri become infected appears to be incorrect.

I believe that most of the bacterial incidence data greatly overstate the problem of postpartum uterine infection in cattle. Probably culture data are not reliable unless the uterine samples are collected by laparotomy or at a careful necropsy to avoid contamination. Organisms from the vagina are frequently drawn into the uterus during slaughter, especially when the cervical canal is open.

Ewe

Involution of the ovine uterus has been described by Uren (1935) and van Wyck *et al.* (1972a,b). Uren concluded that uterine involution was complete at 30 days postpartum. In their first article, van Wyck *et al.* stated that uterine involution was complete by Day 30. In their second article, they reported that "from a macroscopic point of view, then, the uterus appears to have completed involution by the 20th to the 24th day postpartum. . . . On the other hand, as shown histologically, the caruncles are covered with epithelium only by the 28th day." Call *et al.* (1976) concluded that uterine involution "was generally complete by Day 24."

Foote and Call (1969) reported that the total uterine weights for "lactating ewes were 1,256, 1,088, 261, 106 and 96 gm for Day 0, 3, 10, 17 and 24, respectively." They did not mention how the uteri were trimmed. None of the cited references mentioned bacteriologic examination of the postpartum ovine uterus.

I have examined the reproductive tracts from 30 ewes that were slaughtered at intervals from 2 hours through 49 days following parturition. The uteri were cultured for bacteria and fungi and trimmed according to the procedure described for the bovine reproductive tract. The uterine and cervical weights and the character of the uterine content of 17 two-year-old ewes are presented in Table 9.2. Bacteria and fungi were not isolated from any of the uteri.

The weights of the uterine horns ranged from 609 to 1035 g during the first 3 days postpartum. The average uterine weights at 7, 14, 21, 28, 35, and 42 days were 258.8, 219.5, 82.5. 30.5, 28.5, and 20.5 g, respectively.

The placenta was usually expelled within 2 to 4 hours following parturition. In contrast to the cow, very little fluid was present in the postpartum ovine uterus. A small amount of bright red blood was present in the uterine lumen during the first 8 to 10 hours, and this turned dark brown by 12 hours. Some of the caruncles were flat and others cup-shaped during the first 12 hours. It appeared that the separation of the fetal placenta caused eversion of some of the cup-shaped caruncles.

At 12 hours and Day 3 postpartum, the caruncles were cup-shaped (Fig. 9.6) and pale grey, and wedge-

Table 9.2
Postpartum Uterine Involution in the Ewe

Day	Accession Number	Number of Lambs	Uterine Weight (g) L. Horn	R. Horn	Total	Cervical Weight	Uterine Content
1/2	8666	1	354	256	610	62	Small amount of dark brown, tenacious material around cupped caruncles
3	8644	1	202	407	609	67	Small amount of dark brown, thick material around cupped caruncles
3	8682	2	523	512	1035	56	Small amount of dark brown, thick material around cupped caruncles
3	8683	1	250	480	730	48	Small amount of dark brown, thick material around cupped caruncles
7	8635	1	115	230	345	30	Caruncles necrotic and flattened; small amount of thick, dark brown material around caruncles
7	8637	1	44	127	171	18.5	Caruncles necrotic and flattened; small amount of thick, dark brown material around caruncles
14	8636	1	110	181	291	34	Similar to Day 7, but necrotic caruncular tissue can be removed easily
14	8694	1	59	89	148	29	Similar to Day 7, but necrotic caruncular tissue can be removed easily
21	8673	1	20	42	62	10	Similar to Day 7, but necrotic caruncular tissue can be removed easily
22	8701	2	49	54	103	29	Moist, tan-brown necrotic caruncles
28	8672	1	12	14	26	10	No content
28	8780	1	14	21	35	12.5	Small amount of clear mucus
35	8793	1	12	16	28	10	Small amount of clear mucus
35	8798	2	14	15	29	9.5	No content
42	8839	1	12	10	22	12	No content
42	8878	1	9	10	19	10	No content
49	8833	1	10	10	20	11.5	Small amount of clear mucus

shaped areas of hemorrhage extended into some of the decidual caruncular tissue.

By Day 7 and continuing through Day 21, the necrotic portions of the caruncles were dull red, flattened, and covered by dark brown, tenacious material (Fig. 9.7). The necrotic tissue could be removed easily on Days 14 and 21. The vascular stalks of the caruncles were edematous on Day 7.

The uterus was empty, except for a small amount of clear mucus in all ewes slaughtered between Days 28 and 49. Many of the ewes had focal brown areas in the endometrium, especially near the uterine body. This discoloration was due to blood pigment from hemorrhage secondary to trauma sustained during parturition. Irregular-shaped, linear white areas were present in the intercaruncular tissue in some of the ewes slaughtered between Days 28 and 42. Progressive reduction in the size of the uterus occurred up to Day 42. It appears from these observations that the ovine uterus is not completely involuted by Days 24 to 30 as reported in the literature. Most of the reported studies have not extended beyond Day 30 postpartum.

Day 1—Twelve Ewes Were Slaughtered on the Following Hours Postpartum: 2 (Acc. Nos. 7922, 7925, and 7931), 5 (7916), 6 (7914 and 7926), 10 (7915), 12 (7911 and 8666), 15 (7913), 17 (7928), and 18 (7927)

The surface of the caruncles was covered by blood from hematomas that had ruptured during expulsion of the fetal membranes. Hematomas are a normal feature of the placentome of sheep. Maternal blood is extravasated between the chorionic villi and the apical segments of the intercryptal septa of the caruncle (Wimsatt, 1950). The crypts were lined by maternal syncytium with numerous clusters of tightly packed nuclei. A few binucleate trophoblast cells and cellular debris were present between the septa. A zone of hyaline connective tissue was present at the base of the septa.

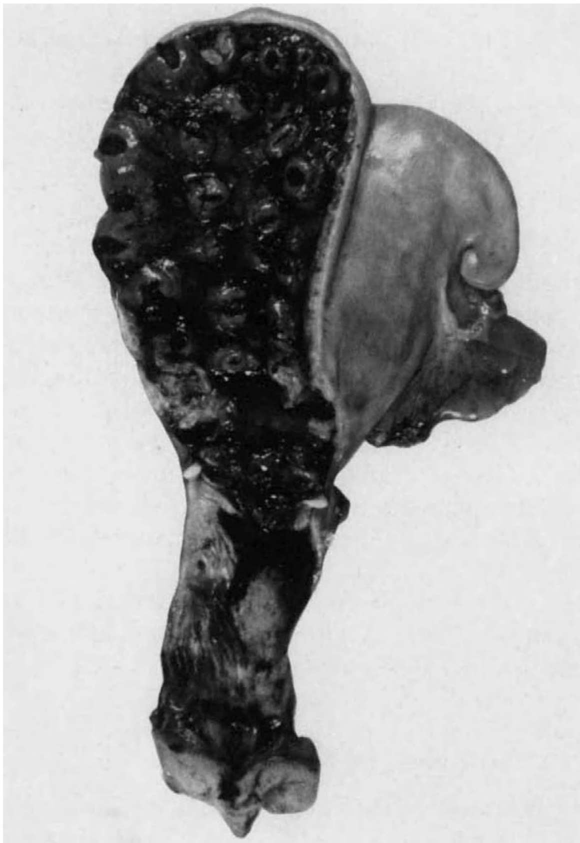

Fig. 9.6. Twelve-hour postpartum ovine uterus with small amount of blood in the uterine lumen, cervix, and vagina. Acc. No. 8666.

Fig. 9.7. Seven-day postpartum ovine uterus with dark brown tenacious material in the uterine lumen and cervix. Acc. No. 8635.

van Wyck *et al.* (1972a) stated that "A histological study of the placentome of the ewe before and during parturition revealed that shortly before parturition the connective tissue of the proximal areas of the maternal villi and adjacent caruncular tissue becomes hyalinized." Uren (1935) reported that at approximately 12 hours after parturition "all of the blood vessels in the area of hyaline degeneration on the inner side of the placental matrix band, and in the crypt mass, are thrombosed."

Thrombi were not seen in the uterine caruncles that I examined during the first 18 hours postpartum. There was vacuolation of the cytoplasm and pyknosis and karyorrhexis of many cells in the media of the thick-walled arterioles in the caruncula septa. Reduction of blood flow to the caruncles in the early postpartum period may be due to the constriction of arterioles supplying the caruncles. Makowski (1968) reported that the radial arterioles of the caruncle have a thick muscular wall and that similar aterioles are not found elsewhere in the uterus. A localized area of constriction of the arterioles is present along the base and periphery of the caruncle before penetrating the septal area. The arterioles are dilated beyond the area of localized constriction. He suggested that the constrictions of the arterioles probably serve as sphincters that regulate maternal blood flow through the caruncle.

The surface epithelium was intact in the intercaruncular area and on the edge of the caruncles up to the area of the previous junction between the chorionic villi and the caruncular septa. Denuded epithelium was not seen at any time during the process of uterine involution. The surface epithelium and the underlying zona compacta were arranged in coarse folds that became more prominent at 6 hours postpartum. The surface of the endometrium and the uterine glands were lined by tall, columnar epithelium.

Numerous degenerating cells were present in the basal portion of the glandular epithelium. The uterine glands were widely dilated at 2 hours and became somewhat collapsed as the interval from parturition to slaughter increased. Neutrophils were present in the uterine glands in 4 of the 12 uteri.

Day 2 (Acc. Nos. 7920 and 7921)

The superficial portions of caruncular septa were necrotic. Many of the nuclei of the maternal syncytium were pyknotic, and cellular debris was present between the septa. Fresh thrombi were present in the septal arterioles and numerous red blood cells were present in the spaces between the septa. A few foci of mineralization were present in the hyaline zone.

The surface epithelium and the compact zone were markedly folded. The uterus of ewe 7920 had numerous neutrophils in the glandular lumen and a scattering of neutrophils in the surrounding stroma. Numerous degenerate cells were present in the basal portions of the glands. Ewe 7921 had a very mild neutrophilic reaction and a few degenerate cells in the glandular epithelium. A moderate number of lymphocytes were present in the glandular epithelium and in the surrounding connective tissue.

Day 3 (Acc. Nos. 8682, 8683, and 8686)

The distal one-fourth to one-third of the caruncular septa were necrotic. Hemorrhagic infarcts extended into the septal mass as far as the hyaline zone of connective tissue. Thrombi were present in arterioles in the hyaline zone adjacent to the infarcts. The degenerative arteriolar lesions were similar to but more advanced than those seen on Day 2. A few arterioles had fibrinoid necrosis. A few areas of mineralization were present in the hyaline zone. Most of the maternal epithelial syncytium was degenerate with numerous areas of detachment of necrotic tissue.

The surface epithelium and associated compact zone were folded into the uterine lumen. The zona compacta was narrow and contained macrophages and a few lymphocytes. Dense hyaline material surrounded the capillaries.

The lumina of the endometrial glands were smaller than on Day 2. Abundant cellular debris and neutrophils were present in the glandular lumina. Vacuoles containing cellular debris were present in the basal portions of the epithelium, and a few neutrophils were presentin the surrounding stroma.

Day 7 (Acc. Nos. 8635 and 8637)

Necrosis of all the septal tissue of the caruncles had occurred except for the large arterioles and the basal hyaline zone in one ewe. The septal mass including the arterioles was necrotic in the other ewe. Focal areas of epithelial proliferation were present in the hyaline zone. A zone of proliferation of stromal tissue was located under the zone of hyaline connective tissue. The vascular stalks of the caruncles were very edematous.

The surface epithelium and the zona compacta were arranged in low, wavy folds. Numerous macrophages were present in the zona compacta, some had vaculoated cytoplasm, and others had brown, coarsely granular cytoplasmic pigment. Dense bands of collagen fibers were present in few areas under the surface epithelium.

The endometrial glands had small lumina and contained cellular debris. Numerous lymphocytes were present in the basal portion of the glandular epithelium and a scattering of lymphocytes, and a few neutrophils and plasma cells, were present in the interstitial tissue. The tunica propria had marked edema.

Day 8 (Acc. Nos. 8630 and 8671)

The septal mass of the caruncles down to the hyaline basal zone, which had irregularly shaped areas of mineralization, was necrotic. There was more extensive regeneration of connective tissue underlying the hyaline zone and more advanced regeneration of epithelium covering the basal portions of the septa than on Day 7. The arterioles and arteries in the vascular stalk of the caruncles had a pronounced increase of loosely arranged, pale blue-staining material in the intima.

The intercaruncular endometrium was similar to that seen on Day 7. Pigmented macrophages were present through the tunica propria.

Day 14 (Acc. Nos. 8636 and 8694)

The appearance of the caruncles was similar to that seen on Days 7 and 8 with the major exception that the edema in the vascular stalks had subsided considerably. The lymphatics in these areas were still very prominent.

The tips of the low, wavy folds of the surface epithelium had papillary proliferations. A few plasma cells and macrophages were present in the zona compacta. Less collagen was present in the zona compacta than on Day 7. The endometrial glands were similar to those of the Day 7 and 8 uteri.

Day 21 (Acc. Nos. 8673 and 8701)

The necrotic caruncular tissue was still attached in ewe number 8673 and the surface epithelium had not regenerated. The necrotic caruncular tissue was detached in ewe number 8701 and the caruncular surfaces were completely covered by epithelium. In this ewe, numerous macrophages and lymphocytes were present in the connective tissue beneath the surface epithelium. A wide zone of normal-appearing stromal tissue was present in the caruncles of both ewes.

The surface epithelium and the compact zone of the intercaruncular endometrium were arranged in low, broad folds. The tops of the epithelial folds had papillary proliferations. Moderate numbers of lymphocytes were present in the glandular epithelium, and there were periglandular accumulations of lymphocytes.

Day 28 (Acc. Nos. 8672 and 8780)

Necrotic caruncular tissue had been eliminated from the uterus and the caruncles were covered by epithelium. A moderate number of lymphocytes were present in the caruncular stroma near the surface epithelium and a few lymphocytes and pigmented macrophages were scattered through the rest of the stroma. Perivascular accumulations of lymphocytes were found around some of the arteries in the vascular stalk. The large veins in the stalk had thick collagenous walls.

No folding of the surface epithelium of the intercaruncular endometrium was evident, in contrast to the earlier postpartum uteri. Numerous, large, multifocal foci of intimately apposed, polyhedral cells with abundant, pale, eosinophilic, finely granular cytoplasm were located in the zona compacta. Golden brown pigment granules were present in some of these cells. The nuclei of the affected cells were similar to but much larger than those of the adjacent stromal cells. The large cells resembled steroid-producing cells, but I am not aware of reports concerning steroid production by the stromal cells of the zona compacta. Another possible explanation for the function of the large cells is that they may be phagocytic. Similar cells, referred to as foam cells, have been reported in the human endometrium. Fechner *et al.* (1979) described the ultrastructure of these cells in the uterus of a 68-year-old woman who had been treated with diethylstilbestrol, 5 mg three times a day for 7 years. Numerous large foam cells, with the ultrastructural characteristics of endometrial stromal cells, were present in the hyperplastic endometrium. The foamy appearance of the cells was due to the presence of lipid droplets. "The droplets were not membrane-limited, and did not appear to originate within any organelle" (Fechner *et al.*, 1979). They stated that "with the exception of one reported case of pyometra, foam cells have been described to occur only in association with endometrial polyps, hyperplasia or adenocarcinoma. These cells can be viewed as the stromal manifestation of unopposed estrogen stimulation." They suggested that "the lipid in the stromal cells is synthesized in response to the stimulus of estrogen." The lesion was found in the uterus of ewe 8672, which also had grossly visible, irregularly shaped, linear white areas in the intercaruncular endometrium. These gross and microscopic lesions were not seen in ewe 8780.

A moderate number of lymphocytes were present in the surface epithelium, in the basal portion of the glandular epithelium, and in the surrounding stroma. A few pyknotic cells were present in some of the glands. A few macrophages containing pale brown cytoplasmic pigment were scattered throughout the tunica propria.

Day 35 (Acc. Nos. 8793 and 8798)

The histology of the caruncles and intercaruncular tissue was similar to that seen on Day 28. Ewe 8798 had foci of large foam cells similar to those in ewe 8672.

Day 42 (Acc. Nos. 8839 and 8878) and Day 49 (Acc. Nos. 8833 and 8870)

The histology of the uterus was similar on Days 42 and 49. There was a slight reduction in the lymphocytic infiltrates from Days 28 and 35. A few large focal accumulations of hemosiderin-laden macrophages were present and were considered to have accumulated because of injuries sustained during parturition. The uteri were not considered to have returned to a normal pregravid condition.

Uterine involution in the ewe differs from that in the cow in several major respects. It requires a longer period of time. It is an aseptic, relatively dry process in which the necrotic septal tissue sloughs as an intact mass. The cervix remains patent for a longer period than in the cow to permit elimination of the intact necrotic caruncular material. Sloughed caruncles can be found in the pasture of bedding as flat masses of compact, necrotic tissue, the shape of which somewhat resembles flukes.

Doe (Goat)

Tielgy *et al.* (1982) described uterine involution in goats slaughtered in pairs at 0, 24, and 62 hours and 5, 7, 9, 12, 15, 18, 21, 25, 28, 32, and 36 days after parturition. The gross changes in the uterus appeared to be similar to those in the postpartum ewe. Culture of the uterine content and histologic changes in the endometrium were not mentioned.

Baru *et al.* (1983) presented a brief discussion of the changes that occur in the caprine uterus during postpartum involution. The article was illustrated with color photographs of uteri at Day 0 through Day 35 following parturition.

Sow

Jones (1966) recorded the characteristics of the postpartum vulvar discharge in sows. "Apart from the fluid expelled from the uterus at, and shortly after delivery, and in conjunction with expulsion of fetal membranes, a vulvar discharge persisted for upwards of a week after parturition in two-thirds of the sows. This discharge was usually mucoid, rather tenacious, often clear at first, gradually becoming streaked by cream or yellow flecks, until eventually the discharge was of a uniformly creamy appearance; it was sometimes tinged brown by altered blood." A variety of bacteria, including *E. coli*, hemolytic streptococci, and unidentified diptheroids, were isolated from the vulvar discharge of 17 clinically normal, postpartum sows. It was emphasized that "care must be exercised in attributing significance to these organisms as causal agents of puerperal disease."

The gross and microscopic changes in the involuting uterus of the postpartum sow have been described by Palmer *et al.* (1965a,b) and Graves *et al.* (1967). According to Palmer *et al.* (1965a), "the uterine weight and length data indicate that the uterus of the sow has involuted by 21 to 28 days after parturition." The length of the uterus decreased from approximately 240 cm on Day 1 to 120 cm on Day 28. The uterine weight decreased from about 2725 g on Day 1 to 244 g on Day 28. Graves *et al.* stated that "myometrial involution appears to have been the result of both cell destruction and atrophy of the muscle cells and interspersing connective tissue."

Palmer *et al.* (1965b) conducted histologic examinations of the ovaries, uterus, uterine tubes, cervix, and vagina from 40 lactating sows slaughtered at 1, 3, 7, 14, 21, 28, 35, 42, and 62 days postpartum. They reported that "At one day postpartum, the gland cells were only 12 to 15 microns high and most were vacuolated with shrunken and pyknotic nuclei, thus presenting a lacy appearance." This appearance of the glandular cells persisted throughout the 8-week lactation period. The surface epithelium at Day 1 was low columnar to cuboidal and measured 10 to 12 μm in height. The uterine lining was folded and the tunica propria was edematous. At Day 7 postpartum, the surface epithelial cells were 5 to 6 μm high and had deeply staining cytoplasm and pyknotic nuclei. Numerous mitotic figures were present in focal areas, indicating regeneration of the epithelium. Numerous leukocytes were present in the stroma underlying the epithelial surface, and the edema of the tunica propria had subsided considerably. The surface epithelium was 15 to 20 μm high and pseudostratified at Day 14. Numerous leukocytes were migrating through the surface epithelium and were present in the subepithelial stroma. At Day 21 the surface epithelial cells were pseudostratified and up to 25 μm high. The leukocytic migration into the uterine lumen had subsided. Relatively little change was noted in the epithelium throughout the rest of lactation.

Mare

Ginther (1979) defined the postpartum interval or puerperium in the mare as "the interval from parturition to the return to a condition conducive to the initiation and maintenance of another pregnancy. The uterus involutes during this time and the ovaries change from a relatively quiescent to an active state." He stated that the "Reported mean lengths of the interval from parturition to the start of the first postpartum estrus are generally given as seven to nine days, and the great majority of mares (>90%) begin estrus within five to 12 days."

Andrews and McKenzie (1941) recorded the first detailed description of the histologic changes in the uterine mucosa of the mare following parturition. They reported that the uterus of only one out of nine mares had returned to a normal pregravid state on the first day of estrus. They stated that "In some cases the mucosa appeared to be completely restored to the farrow (pregravid) condition by the third or fifth day of estrus, and in others involution seemed to continue until about the fifth day of the interestrual period."

Gygax *et al.* (1979) investigated the bacteriologic, histologic, and endocrinologic changes associated with postpartum involution of the uterus in seven mares. Samples of cervical and endometrial content were cultured for bacteria, endometrial tissue was collected for biopsy, and blood plasma was assayed for progesterone levels. Progesterone was "non-detectable from the day after parturition until the rise, usually associated with ovulation and the formation of the corpus luteum." Beta-hemolytic streptococci and coliform bacilli were recovered throughout the experimental period, which extended through Day 32 postpartum. No correlation was found between positive cultures of endometrial swabs and histologic evidence of inflammation, and they suggested that the frequent swabbing of the endometrium and the taking of biopsy specimens may have caused contamination of the endometrium. By Day 1 postpartum, the endometrial glands were distended and the stromal tissue was edematous. The microcaruncles extended from the luminal surface into the stratum spongiosa. The epithelium of the microcaruncles had cytoplasmic vacuolization and focal areas of karyorrhexis. Hemorrhagic and nonhemorrhagic microcaruncles were present in the early postpartum period. Some of the maternal crypts underwent cytoplasmic vacuolization, karyorrhexis, and cellular lysis while others involuted by shrinkage of the maternal epithelial cells and collapse of the cryptal lumina, resulting in shrinkage of the entire microcaruncle. Most of the microcaruncles underwent involution without an inflammatory reaction. The microcaruncles were no longer evident by Days 6 or 7 postpartum except for some "small focal remnants consisting of condensed stroma and crypts lined by contracted or vacuolated epithelial cells. . . . After Day 7 the sites of the former microcaruncles were marked either by areas of stratum compactum of low cell density or by aggregations of macrophages" (Gygax *et al.*, 1979). The endometrium appeared to be quite normal by Day 14 "except for occasional slight pleomorphism of the luminal epithelium, the sporadic occurrence of inflammatory changes and the presence of foci of siderocytes."

Steven *et al.* (1979) investigated the ultrastructural features of the placenta and postpartum uterus of the mare. They concluded that "uterine involution is well advanced by the 3rd and 4th days postpartum and the changes are usually complete by the oestrous, 7 to 10 days after parturition."

Vandeplassche *et al.* (1983) stated that involution of the equine uterus starts immediately following expulsion of the foal and "is characterized by a rapid and marked contraction of the uterus, the cervix, the vagina and the broad ligaments. Consequently, the size of the genital tract rapidly regresses so that about 12 hours postpartum, the uterine horn that was pregnant is not more than 1.5 times the size of the nonpregnant horn." The weight of the uterus changed very little during the first 2 days following parturition. "The uterus and cervix of ten mares, each of which died or were slaughtered within two days postpartum, weighed between 7 and 9 kg. . . . About Day 8 postpartum, the uterine weight is about 2 kg" (Vandeplassche *et al.*, 1983).

Bitch

Anderson and Simpson (1973) described the histology and Al-Bassam *et al.* (1981) recorded the gross and microscopic changes in the canine uterus during normal postpartum involution. The following description is in reference to the latter report.

During the first week following parturition, small longitudinal folds were present in the serosa of the edematous, dilated uterus. The placental sites were rough, granular, and covered by dark brown mucus and blood clots. The mucosa between the placental sites was folded and covered by dark brown mucus.

A gradual reduction in the size of the uterus occurred during the second and third weeks. The placental sites were gray-tan and contained blood clots. The entire mucosal surface was covered by dark brown mucus.

The uterus was much smaller by the fourth week. The placental sites were gray-tan and contained 2- to 4-mm gray nodules with a few small petechial hemorrhages and blood clots. The interplacental endometrium was covered by clear mucus. During the fifth to eighth weeks, the size of the uterus was reduced, and it reached its smallest size by the eighth week. The numbers and size of the gray nodules in the placental sites were reduced. The uterine horns were uniform in shape by the ninth week, and the placental sites were differentiated from the rest of the endometrium by their brown color.

Placental Sites

In regard to the histology of the postpartum uterus, Al-Bassam *et al.* (1981) stated that "after separation of the placenta, the basal glandular zone was the only viable and intact layer remaining. At the place of placental separation over the basal glandular zone, a necrotic mass was observed with a few intact, large and foamy epithelial cells scattered on the surface as an interrupted single layer." The necrotic mass consisted of "remnants of fetal placenta, fragments of the separated spongy layer, fibrin, erythrocytes, necrotic thrombosed blood vessels and nuclear debris." Large acidophilic, polygonal cells with one to two large nuclei were present in the lamina propria. Many of these cells had pyknotic nuclei and vacuolated, basophilic cytoplasm. They stated that "these cells were considered to be either decidual cells (maternal) or trophoblastic cells (fetal), but due to their greater similarity to decidual cells have been designated as decidual cells."

This conclusion may not be warranted. In cases of subinvolution of placental sites, these cells persist and are invasive in some cases, which suggests that they are trophoblastic cells. Immunohistochemical studies should be conducted to establish the true identity of the large acidophilic cells.

Mossman (1987) stated that "Because nothing is known of the function of these cells in carnivores, and they are not in the position of typical decidua, I consider the term 'decidual cells' unfortunate. . . . Until more is known about these cells and a more accurately descriptive term can be coined, 'maternal giant cell' seems preferable."

Al-Bassam *et al.* (1981) reported that lobulated masses of collagen formed in the placental sites during the second week and small hemorrhages and scattered mononuclear cells were present in the lamina propria. Most of the "decidual" cells were degenerate. The amount of collagen covering the placental sites increased during the third week. Mononuclear cells, consisting of macrophages, lymphocytes, and plasma cells, were greatly increased in the lamina propria. The endometrial glands contained cellular debris and erythrocytes. A few degenerate "decidual" cells were present in only two out of eight uteri.

The lobulated masses of collagen in the placental sites reached their largest size by the fourth week. The surface of the masses was necrotic and hemorrhagic. The persisting surface epithelium consisted of foamy, columnar epithelial cells. The endometrial glands contained mucus and sparse necrotic debris. A pronounced mononuclear cell infiltrate was present in the lamina propria.

Al-Bassam *et al.* (1981) stated that "by the beginning of the fifth week, the last and most important stage of placental site involution started with the massive denudation of the collagen masses into the lumen. . . . The area of detachment was soon regenerated and covered by a single layer of columnar epithelial cells." Macrophages, lymphocytes, and a few plasma cells were present around the uterine glands and under the surface epithelium. "Changes similar to those observed during the fifth week were seen during the sixth and seventh week postpartum but were more prominent. Most of the collagen masses were detached from the endometrium and found in the uterine lumen" (Al-Bassam *et al.*, 1981).

The sloughing of necrotic tissue was complete by the ninth week, "but the regeneration of endometrial epithelium continued from the mouth of the uterine glands and from the regenerated epithelial cells on the surface. This process continued until the end of the twelfth week when the whole endometrium was lined by a single layer of small cuboidal or columnar cells with basophilic cytoplasm and darkly stained basal nuclei" (Al-Bassam *et al.*, 1981). The placental sites were brown owing to the presence of hemosiderin-laden macrophages.

Interplacental Site Endometrium

During the first week, primary and secondary folds of the surface epithelium were present. The epithelial cells had a foamy cytoplasm due to the presence of lipid droplets. The lamina propria was edematous and contained a few lymphocytes and plasma cells. "By the fourth week, massive sloughing of epithelial cells (surface epithelium) occurred into the lumen" (Al-Bassam *et al.*, 1981). The number of mononuclear cells increased in the lamina propria, which was less edematous. Some of the endometrial glands were slightly dilated while the rest were small and lined by cuboidal to low columnar epithelial cells.

Sloughing of the surface epithelium continued during the fifth and sixth weeks, and only small folds of foamy cells covered the endometrium. Numerous fibroblasts, macrophages, plasma cells and a few neutrophils were present in the lamina propria.

Exfoliation of degenerate, foamy, surface epithelial cells and regeneration of epithelium from the necks of endometrial glands continued during the seventh and eighth weeks. "By the ninth week, many areas of the endometrium were replaced by a single layer of small cells with basophilic staining cytoplasm. . . . by the end of the twelfth week the whole endometrium was lined by a single layer of small cuboidal or columnar cells with basophilic staining cytoplasm" (Al-Bassam *et al.*, 1981). The authors concluded that 12 weeks are necessary for completion of uterine involution in the bitch.

Queen

Dawson (1946) described the histologic changes that occur during postpartum involution of the feline uterus. Following parturition the placental sites consisted of residual connective tissue of the lamina propria and the bases of the uterine glands. The interplacental site endometrium had a complex luminal surface "composed of papilliform and plate-like projections" that had developed during pregnancy.

Placental Sites

The basal portion of the endometrium, which remained after delivery of the placenta, was infiltrated with neutrophils and macrophages. Replacement of the surface epithelium occurred by proliferation of the basal portions of the endometrial glands and, to a lesser extent, by in-growth of epithelium from the interplacental site endometrium. "Large, multinucleated masses, with densely stained and closely grouped nuclei, were frequently found on the surface of the healing endometrium . . . these represent vestiges of the implantation reaction and some persisted in the endometrium until at least 15 days after parturition" (Dawson, 1946). Dawson concluded that "these multinucleated elements are probably identical with the symplasmal masses of the cat's placenta described by Wislocki and Dempsey (1946)."

Interplacental Site Endometrium

Gros (1935) reported that a leukocytic infiltration of the endometrium of the cat occurs during the last weeks of pregnancy. The leukocytic infiltrate increases and the surface epithelium degenerates after parturition. He stated that the uterus is usually free of cellular debris at the end of the sixth day.

According to Dawson (1946), "the time of onset and degree of desquamation of the surface epithelium were variable. Some of the tips of the projections exhibited advanced involution as early as ten hours after delivery of the last kitten, although intact epithelium was found in some locations as late as 48 hours postpartum." In some of the low folds, involution occurred without sloughing of the epithelium.

The endometrial glands were dilated at the termination of pregnancy. Some of the glands were empty and others contained acidophilic material. "Numerous mitotic figures were present in the glandular epithelium at ten hours after delivery, the earliest postpartum stage studied. At the end of the sixth day, the surface of the uterus was completely covered by a low cuboidal epithelium" (Dawson, 1946).

Dawson stated that "after the end of the first postpartum week the changes in the endometrium became almost entirely restorative rather than retrogressive." The uterine glands increased in length and numbers, and the stroma transformed from a loose fibrous tissue into a compact cellular stroma.

Ovarian follicles began to develop at the end of the second postpartum week in nonlactating cats, and "the uterus soon regained its normal appearance and size. The cornua lost their flattened form and became cylindrical." Estrus was observed in two non-lactating cats at the end of the fourth postpartum week.

Dawson also stated that "After the beginning of the fourth week, both the myometrium and the endometrium exhibited progressive involution and these retrograde changes continued until lactation ceased." The uteri at this time resembled those of cats that had been castrated for comparable periods. The "hyperinvolution" was associated with ovarian inactivity during lactation.

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Chapter 10

The Uterus: Degenerative and Inflammatory Lesions

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- Hemorrhage Associated with Uterine Subinvolution and Infection
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Bibliography

Vascular Lesions

Hyperemia and Hemorrhage Associated with Estrus

The tunica propria of the endometrium becomes hyperemic and edematous several days before the onset of estrus in all species of domestic mammals. Metestrual hemorrhage in the endometrium, which is common in heifers and less common in cows, is discussed in Chapter 7. A second episode of hyperemia and a small amount of hemorrhage occurs in cows at Days 8 to 10 of the estrous cycle when the midcycle follicle is enlarging.

Petechial to diffuse hemorrhages occur in the uterine subserosa of virgin heifers during and a few days after estrus. Weber *et al.* (1949) reported that "Fifteen of 17 heifers slaughtered during estrus to four days postestrus showed grossly evident perimetrial hemorrhages. The hemorrhages ranged from a few scattered petechia on the greater curvature of the uterine horns and dorsal aspect of the body of the uterus to massive petechial, ecchymotic and diffuse hemorrhages in these areas." Subserosal hemorrhages were not seen during any other stages of the estrous cycle in heifers nor in cows at any stage of the cycle. "Evidence of capillary and arteriole rupture was noted. The erythrocytes appeared to be discretely scattered in the connective tissue. Very few neutrophils and macrophages were observed, although mast cells were numerous" (Weber *et al.*, 1949).

Marked edema and hyperemia occur in the lamina propria of the canine uterus by the first day of proestrus. Hyperemia is evident in the capillaries immediately beneath the surface epithelium. Focal areas of extravasation of erythrocytes occur into the subepithelial connective tissue. Evans and Cole (1931) prepared serial sections of the areas of extravasation without finding any break in the continuity of the epithelium. They stated that "The bleeding points are either very few in number or very minute for we have carefully opened both uterine horns of an animal showing abundance of blood at the vulva, and have been astonished to make out no rupture points from which the hemorrhage could have proceeded."

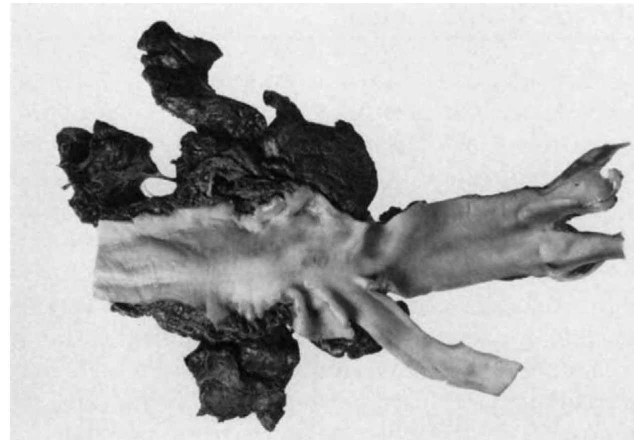

Fig. 10.1. Ruptured middle uterine artery from a cow that died of hemorrhage 5 days postpartum. Acc. No. 1194.

Hemorrhage Associated with Uterine Subinvolution and Infection

Abnormal uterine bleeding is associated with subinvolution of the placental sites. It can also occur with the progesterone-induced cystic hyperplasia–pyometra complex in the bitch.

Vascular Lesions Associated with Pregnancy and the Puerperium

Effusions of maternal blood are characteristic of the margins of the placenta of the dog and the cat. In the dog the hemorrhages "occur regularly along the margins of the placental zone, but in addition, smaller hemorrhages take place into the substance of the placenta and form the 'green pockets' or central hematoma. In the cat and coati, supernumerary 'pockets' are sometimes found in the form of 'chorionic vesicles' that are entirely lined by trophoblast" (Amoroso, 1952). The hematomas "separate the trophoblast from the underlying maternal tissues and deflect it in the form of irregular pouches toward the interior of the chorionic sac" (Steven, 1975). The breakdown products of hemoglobin are responsible for the green-brown appearance of the placental margins in these species.

The formation of superficial hematomas is a characteristic feature of the placentome of the ewe. Maternal blood "is extravasated copiously between the chorion and the apical segments of the intercryptal septa" (Wimsatt, 1950).

"In 12- to 21-year-old mares, rupture of the uterine vessels and sudden death due to hemorrhagic shock may occur before, during or after the apparent normal gestation and parturition. The middle uterine artery was most commonly involved but the iliac or utero-ovarian arteries occasionally were affected" (Roberts, 1971).

Fatal hemorrhage due to rupture of uterine arteries also occurs in the cow. A cow, which was 5 days postpartum, appeared normal at milking time. After milking the cow trembled, fell down, and died within 2 1/2 hours after the first signs were observed. A large volume of clotted blood was present in the peritoneal cavity and a large blood clot was attached to the uterus. A 2.5-cm rupture was present in the left middle uterine artery (Fig. 10.1) about 30 cm from the aorta.

Thrombosis of blood vessels in the placental sites of carnivores and in the caruncles of postpartum ruminants is normal.

Age-associated uterine changes have been reported in the cow (Mochow and Olds, 1966), the bitch (Stott, 1970), and the sow (Bal and Getty, 1973). Significant vascular lesions occur in the uterus of aged cows and sows and appear to develop as a consequence of repeated pregnancies. Nieberle and Cohrs (1967) referred to the arterial lesions, which occur during postpartum uterine involution, as "physiological pregnancy sclerosis." They stated that "this is so characteristic that it can be used to diagnose an earlier pregnancy with absolute certainty. . . . Histologically, there is reorganization in the vessel wall in the form of hyperplasia of the elastic fibers in the intima and media (elastosis), hyaline changes in connective tissue and atrophy of muscle fibers."

Bal and Getty (1973) examined the reproductive tracts from 44 nonpregnant and 5 pregnant sows between the ages of 1 to 10 years. The endometrial arteries had intimal thickening at 18 months of age and the lesion increased progressively with age. "During pregnancy, elastic tissue in the tunica intima of the endometrial arteries appeared to disappear and reappeared in the postpartum period" (Bal and Getty, 1973). Lipofuscin pigment, which increased with age, was present in the smooth muscle of the venous walls and in the myometrium by the age of two years. Pigment was not found in the smooth muscle cells of arteries.

Uterine Emphysema

Gas bubbles can form in the endometrium, between the compact and glandular zones (Fig. 10.2) of the postpartum cow. The condition does not appear to be due to infection because there is very little or no inflammatory reaction in the uterus. King and Lee (1983) suggested that emphysema of the bovine urinary bladder is caused by the absorption and enzymatic breakdown of sugar following the intravenous injection of glucose. They reported that the condition also occurs in the abomasum of calves given high-sugar-content electrolytes. Perhaps sugar is the cause of emphysema of the uterus in postpartum cows that are treated with intravenous injections of glucose.

Inflammatory Lesions

Endometritis refers to inflammation limited to the endometrium; metritis is involvement of the entire thickness of the uterine wall; perimetritis is inflammation of the uterine serosa; and parametritis is involvement of the tissues surrounding the uterus. The nongravid uterus is relatively resistant to infection although bacteria are always present in the vagina. The cervix is a very efficient protective barrier and often prevents organisms from entering the uterus. The cervical canal is closed during the luteal phase of the estrous cycle. It is only open during estrus when the uterus is under the influence of estrogen and is less susceptible to infection. Most uterine infections begin in the endometrium and are associated with mating, pregnancy, or postpartum uterine involution. They are usually self-limiting in animals with normally developed reproductive tracts. Local antibody production plays a significant role in limiting the duration of most uterine infections.

In cases of endometritis, exudate is present in the uterine lumen (Fig. 10.3). When examining the reproductive tract postmortem, it should be remembered that the endometrium undergoes autolysis very rapidly, resulting in sloughing of the surface epithelium. The sloughed tissue resembles pale tan exudate on gross examination. A smear of the material will indicate whether leukocytes are present or whether it comprises merely desquamated epithelial cells.

Numerous neutrophils are present in the zona compacta and in the surface epithelium during the early stage of endometritis. Subsequently, the inflammation extends into the lumina of endometrial glands (Fig. 10.4) and the surrounding connective tissue becomes infiltrated with lymphocytes, macrophages, and plasma cells. Interstitial lymphocytic foci (Fig. 10.5) develop in the endometrium in association with a variety of infectious agents. In severe inflammation, the necks of some of the endometrial glands become occluded. The underlying glands become dilated, lined by a flattened layer of epithelial cells, and surrounded by a zone of fibrous tissue (Fig. 10.6). Such glands remain cystic after the inflammation subsides.

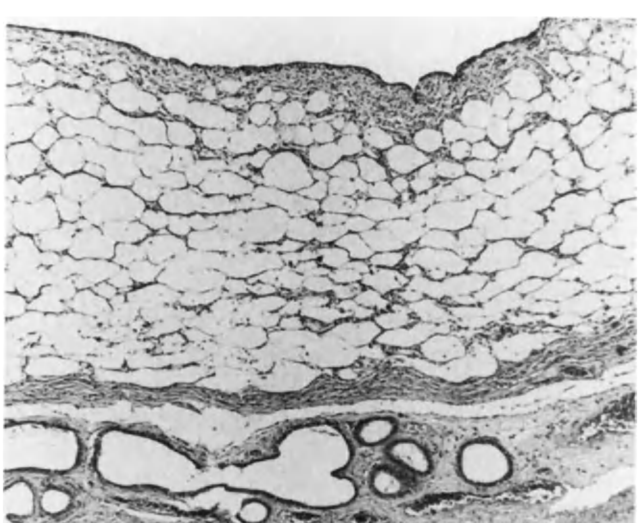

Fig. 10.2. Emphysema of bovine endometrium. The submucosa of the uterus resembled lung on gross examination. ×4. Acc. No. 1196.

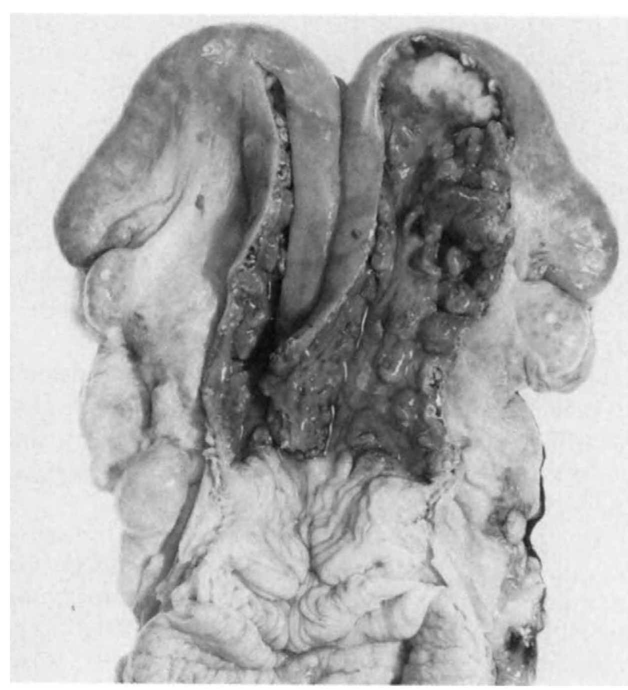

Fig. 10.3. Endometritis with exudate in the cranial part of the right uterine horn of a cow. Acc. No. 11036.

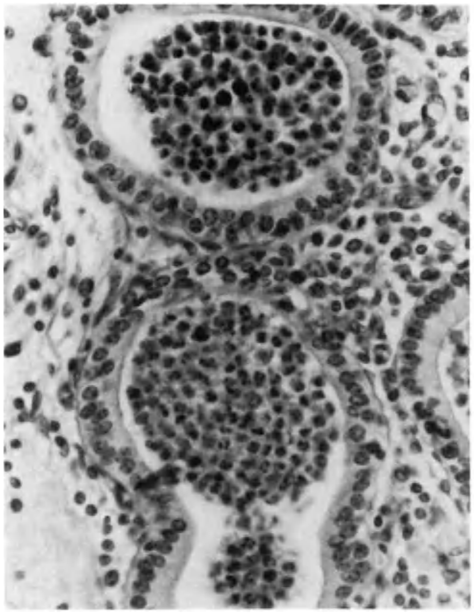

Fig. 10.4. Bovine uterus with neutrophils in the lumen of endometrial glands and periglandular mononuclear cell accumulation due to vibriosis. ×329. Acc. No. 4822.

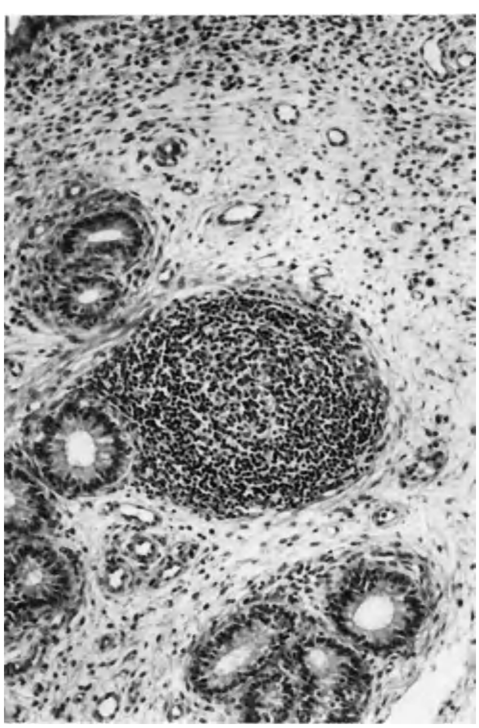

Fig. 10.5. Interstitial lymphocytic nodule associated with vibriosis in a bovine uterus. ×101. Acc. No. 2400.

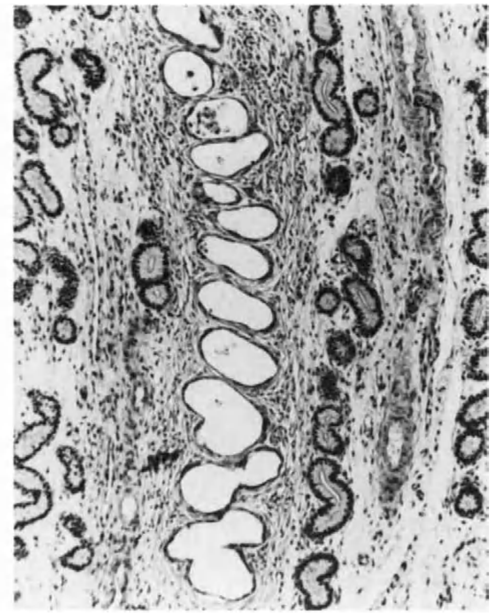

Fig. 10.6. Cystic bovine endometrial gland with flattened epithelium, periglandular fibrosis, and mononuclear cell infiltration. ×66. Acc. No. 2518.

Endometrial Biopsy

The endometrium may be studied by examination of tissue taken for biopsy. (Biopsy refers to the examination of tissue taken from a living animal. You do not take a biopsy, but you take tissue for biopsy.) The Yeoman biopsy punch, with a 15-inch handle, is satisfactory for obtaining specimens of endometrium from cattle. It cuts a larger section of endometrium than most other available instruments and, in fact, it is possible to cut out a section of entire uterine wall, including muscle and serosa. Thus, it is preferable to remove tissue from the ventral or medial uterine wall to avoid uterine perforation. Parametritis and peritonitis may develop if an infected uterus is perforated. A larger biopsy punch is used for obtaining endometrial specimens from the mare. The removal of uterine tissue with a biopsy instrument may result in the production of artifacts, including intussusception of glands, distortion of uterine gland epithelium, denuding of surface epithelium, hemorrhage, and edema. Considerable hemorrhage may occur if a large caruncular artery is cut.

Pyometra

Postcoital Pyometra

Pyometra refers to the accumulation of exudate in the uterine lumen. It may occur following breeding or parturition. Most cases of postbreeding pyometra in cattle are due to *Tritrichomonas (Trichomonas) fetus* infection but trichomoniasis, contrary to popular belief, does not cause pyometra very frequently. In one infected herd that I examined, two cases of pyometra were diagnosed among 169 cows.

The exudate is usually a gray-yellow, watery, practically odorless, alkaline fluid containing small clumps of leukocytes and fetal remnants. The average volume of uterine exudate in 20 cases reported by Morgan and Whitehair (1943) was 1403.7 ml, and "the average number of trichomonads per cc was approximately 1.5 million."

The microscopic lesions consist of dilated endometrial glands, many of which contain neutrophils, and large, multifocal, periglandular foci of lymphocytes, macrophages, and plasma cells. Small abscesses, some of which are visible on gross examination, may be present in the endometrium. The abscesses arise following destruction of glandular epithelium and extension of the suppurative process into the surrounding stroma. Some glands have prominent periglandular fibrosis.

I have seen only one case of postcoital pyometra due to *Campylobacter fetus venerealis* infection in a heifer. I am not aware that it has been reported by others.

Postpartum Pyometra

Cow. Postpartum pyometra in the cow is usually due to *Actinomyces pyogenes (Corynebacterium pyogenes)* and gram-negative anaerobic bacteria, including *Fusobacterium necrophorum* and *Bacteroides melaninogenicus* (Olson *et al.*, 1984a,b). There is generally a large quantity of malodorous exudate in the previously gravid horn. The uterine wall is thicker than normal and receding caruncles may be evident in early cases of infection. A postpartum corpus luteum is present, and the affected cow is usually anestrus. In early cases of pyometra, the inflammatory reaction extends throughout the endometrium, but in long-standing cases, it is restricted to the superficial portion. In these cases, a thick zone of dense, fibrous tissue is present beneath the inflamed area. Multifocal areas of squamous metaplasia may be present in the surface epithelium.

Mare. Hughes *et al.* (1979) reported 16 cases of pyometra in mares. The average age of the mares was 17 years and none showed clinical signs of systemic disease. The quantity of uterine exudate ranged from 0.5 to 60 liters. The character of the exudate was described as watery, creamy, thick cream, or cheesy in different cases. "One or more species of bacteria were isolated from some, but not all uteri. *Streptococcus zooepidemicus* was most commonly found and other organisms included *Escherichia coli, Actinomyces* sp., *Pasteurella* sp., *Pseudomonas* sp. and *Propionibacterium* sp." (Hughes *et al.*, 1979). They reported that "all of the mares had endometritis, but the type and its severity varied among animals, and between different areas of the same uterus. . . . Mostly the endometrial surface was smooth and glistening, but in a few cases where the endometrium had been eroded and the epithelial layer had not regenerated, the surface was rough and finely granular." The lesions were most severe in the body of the uterus in all cases. The estrous cycles were shortened in mares with the least endometrial damage and lengthened in mares with severe endometritis. "In a few animals, there was a complete loss of cyclic luteal function, the largest continuous luteal phase observed being 613 days; no cyclic PGF-2 alpha release patterns were observed in these animals" (Hughes *et al.*, 1979).

Vandeplassche *et al.* (1979) reported a case of pyometra in a 10-year-old mare of unknown breeding history. They stated that "the presence of fully developed endometrial cups in the uterus of a mare and the absence of a foetus or fetal membranes indicate that the mare had been pregnant for at least 40 days before fetal death and loss had occurred." The uterus contained about 3 liters of exudate. The predominant organism was a β-hemolytic *Streptococcus.* A "few *E. coli* and some unidentified gram-positive cocci and coccobacilli" were also isolated.

Bitch and Queen. Most cases of pyometra in the bitch and queen are secondary to progesterone-induced cystic hyperplasia of the endometrium, which is discussed in Chapter 11.

Perimetritis and Parametritis

Perimetritis is inflammation of the uterine serosa, and parametritis refers to inflammation of the tissues around the uterus. These lesions usually occur concurrently and may be due to severe septic metritis, perforation of the uterine wall by a catheter or insemination pipette, perforation of the vaginal wall by the penis, rupture of the uterus during parturition, uterine torsion, and hemorrhage following enucleation of corpora lutea. The lesions are also associated with tuberculosis and epididymitis-vaginitis (epivag) reported from Africa by Daubney *et al.* (1938). Inflammation of the uterine serosa and tissues adjacent to the uterus results in the formation of fibrous adhesions between the uterus and the broad ligaments, omentum, rectum, intestines, bladder, and body wall.

Uterine Abscess

Most of the uterine abscesses that I have seen have occurred in cattle. Large abscesses, up to 30 cm in diameter, have been found in the dorsal portion of the uterine body (Fig. 10.7) or in the dorsal part of one uterine horn a few centimeters cranial to the uterine body. Adhesion of the omentum to the wall of large abscesses occurs frequently. Occasionally, large abscesses adhere to the abdominal wall. They usually contain a creamy, foul-smelling exudate from which pure cultures of *Actinomyces pyogenes* or mixed cultures of *A. pyogenes*, staphylococci, and/or streptococci are isolated. *Pseudomonas aeruginosa* is present in abscesses with thick, pale green, odorless exudate.

Abscesses up to 3 cm in diameter have been found in and beneath caruncles in cows with postpartum endometritis. Microscopic abscesses may be present in the uteri of cattle infected with a variety of bacteria.

Oil Granuloma

The intrauterine infusion of therapeutic agents in an oil-base vehicle occasionally results in the development of a granuloma. When oil is injected into the wall of the uterine body or into the wall of the distal portion of one uterine born in cattle, a focal granuloma develops. If a large volume of oily fluid is infused into the uterine lumen, the uterus may rupture at the mesometrial attachment, allowing the fluid to diffuse into the broad ligament, causing massive granulomas. Vacuolated macrophages, giant cells, and proliferating fibrous tissue are present in the granulomas (Fig. 10.8). Plasma cells are present in some of the lesions.

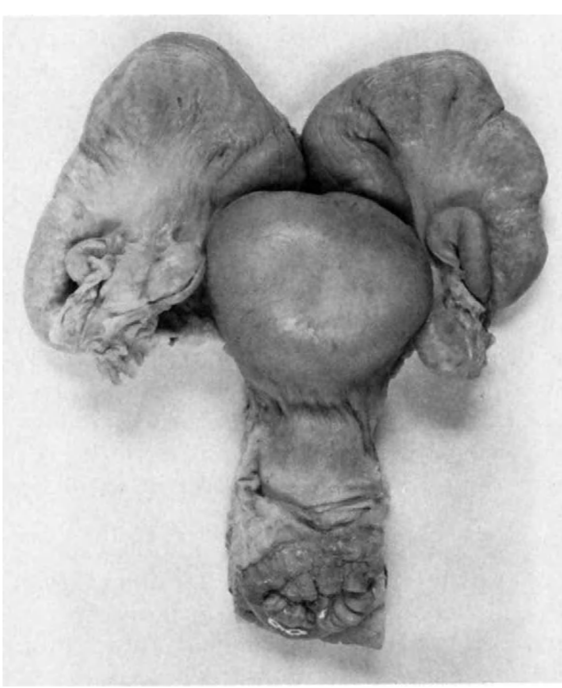

Fig. 10.7. Abscess in the uterine body of a cow. Acc. No. 3557.

Nonspecific Infections

Numerous articles have been published on the isolation of a wide variety of bacteria from the uteri of nongravid and gravid animals. The isolation of bacteria from uteri that are free of inflammatory lesions suggests that the isolates are contaminants or at least that they are nonpathogenic for the uterus. Scott *et al.* (1971) stated that "the reproductive tract can harbour bacteria without the production of pathological change and that the culture of swabs from cervix or uterus of mares is of doubtful value unless there is evidence of disease." Culture results should be correlated with uterine lesions.

Specific Infections

Brucellosis

Cow. The pathology of brucellosis in humans and animals was reviewed by Jacob (1964). It is a systemic disease that is usually acquired by ingestion of *Brucella*-contaminated materials, but also develops following breeding to infected bulls and by conjunctival or skin exposure, especially through breaks in the skin. In regard to the reproductive system of the cow, brucellosis is primarily a disease of the gravid uterus.

Payne (1959) described the uterine lesions in 11

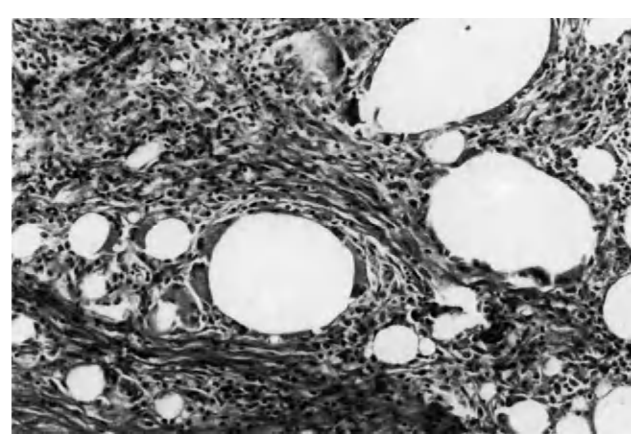

Fig. 10.8. Oil granuloma in the bovine myometrium. ×89. Acc. No. 18636.

pregnant cows that were infected by placing a suspension containing 150 million virulent *Brucella abortus* organisms into the conjunctival sac. The cows were killed at about weekly intervals after infection. Large numbers of organism were isolated from the parotid lymph nodes at 1 week after infection. After 2 weeks, *B. abortus* was isolated from the spleen and supramammary lymph nodes. "After the fourth week *Br. abortus* was consistently isolated, usually in large numbers, from the uterine lumen (intercotyledonary space)" (Payne, 1959).

No histologic changes in the uterus were detected before Day 22 postinfection. After this interval, plasma cells, lymphocytes, neutrophils, and a few eosinophils are present in the connective tissue surrounding endometrial glands. The endometrial glands become filled with exudate. The infection extends from the glands to the surface epithelium, resulting in "severe and extensive ulcerative endometritis. . . . By the time of abortion, nearly all the endometrial mucosa is eroded and replaced by subacute inflammatory granulation tissue" (Payne, 1959). The inflammation extends from the intercaruncular endometrium to the placentomes. "At this site *Br. abortus* induces some ulceration of maternal tissue and multiplies to enormous numbers in chorionic trophoblast cells. These degenerate and die and leave the chorion free in the exudate. . . . Bacteria next invade the connection tissue of the allantochorion and enter the foetal blood vessels" (Payne, 1959).

The bacilli usually disappear from the uterus soon after abortion or parturition, and the infection frequently reappears in the uterus during subsequent pregnancies. It localizes in lymph nodes and mammary glands, which serve as reservoirs of infection between pregnancies. Uterine infection persists in some cows for prolonged periods of time. Birch and Gilman (1931) recovered *B. abortus* from the uterus of four cows that had not been pregnant for 7, 8, 13, and 15 months.

Sow. Brucellosis in the sow is quite different from that of the cow in that nonpregnant as well as pregnant sows have characteristic uterine lesions. "In most cases the inside of the uterus shows numerous whitish-yellow nodules, ranging in size from tiny points to hemp-seed (seldom of pea-size), raised slightly over the surface. . . . On section the nodules are found to be well defined and firm in consistency—sometimes with a little central purulent or caseous focus, in which bacilli as a rule are not demonstrated" (Thomsen, 1934). Usually, the nodules are numerous, may "fuse into plaques appearing almost like a pavement," and may be visible under the serosa. Thomsen designated the lesions as "miliary brucellosis."

Christiansen and Thomsen (1934) described the microscopic uterine lesions in *Brucella*-infected sows. The lumina of the endometrial glands are dilated and filled with cellular debris. There is multifocal necrosis of endometrial glands and the surrounding connective tissue, which is infiltrated with lymphocytes, macrophages, and neutrophils. Multinucleated giant cells are present on the periphery of the necrotic tissue. The lesions are scattered throughout the tunica propria but are most prominent in the superficial portion of the endometrium.

Tuberculosis

The term tuberculosis is derived from the Latin word *tuberculum*, meaning a small lump or nodule. Cattle may become infected with *Mycobacterium bovis*, *M. avium*, or *M. tuberculosis*. The lesions produced by the avian and human strains are comparatively mild in most affected cattle. Boughton (1969) reviewed the literature concerning the occurrence of avian tuberculosis in domestic, captive, and wild birds and mammals. It is often difficult to trace the original source of avian tuberculosis in domestic mammals.

According to Francis (1958), "about 5% of tuberculous cows have tuberculous metritis and although direct infection may occur from tuberculous peritonitis or from the external genitalia, the commonest route of infection in hematogenous, and it nearly always occurs during pregnancy." When the disease is generalized, approximately 20% have uterine lesions. Histologic examination of the uterus in all cows with tuberculosis would probably reveal a higher incidence of uterine infection, because early lesions are not visible on gross examination. Quinlan (1927) found tuberculous lesions in the uterus of 18% of infected cows.

Steward (1941) reported that "Examination of uterine discharge from cows suspected of being affected with tuberculosis is often the easiest method of obtaining a positive diagnosis. . . . In positive cases the discharge is usually scanty and white, yellowish or golden-coloured, though rather transparent, rusty-coloured, positive samples have been seen." Twenty-four of 79 samples of uterine discharge examined microscopically were positive for tubercle bacilli. No definite clinical signs were evident in 19 of the 24 cases.

Pallaske (1965) and Nieberle and Cohrs (1967) described the uterine lesions in cows infected with *M. bovis*. The lesions ranged from small, multifocal, endometrial tubercles (diffuse miliary tuberculosis) to diffuse, caseous necrosis of the endometrium (diffuse caseous endometritis). According to Nieberle and Cohrs, the miliary nodules are "variously distributed, sometimes in large numbers over the entire mucosa, sometimes confined to the cranial end of one or both cornua and sometimes in irregular groups in the body of cornua." The endometrium appears normal on gross examination in the early stage of development of the lesion. As the tubercles enlarge, they appear as small, gray nodules. Large nodules ulcerate and discharge yellow purulent material into the uterine lumen. In caseous endometritis, the uterine horns are thick and rigid (Fig. 10.9). The uterine lumen contains serous fluid with floccules of fibrin or yellow mucopurulent, slimy fluid.

Epithelioid tubercles are present in the miliary form, and most of them are directly below the surface epithelium and in the vicinity of uterine glands (Fig. 10.10). As the tubercles enlarge, they undergo central caseous necrosis, erode the surface epithelium, and may have fibrous encapsulation and mineralization. Tubercles may be present in the myometrium. In caseous endometritis, there is diffuse, caseous necrosis of the endometrium adjacent to the lumen and fingerlike areas of necrosis extend into the deeper areas of the endometrium. Exudative inflammation is associated with the necrosis, and a thick layer of fibrin forms over the caseated areas. A zone of epithelioid cells is present below the necrotic tissue. Nieberle and Cohrs (1967) stated that "caseous endometritis constitutes a reaction of hypersensitivity and is a typical primary caseation."

Mycobacterium avium infection of cattle usually produces mild disease with lesions in various lymph nodes. At one time, it was thought that the lesions were restricted to the mesenteric lymph nodes, but Cassidy *et al.* (1968) found tubercular lesions in the bronchial, suprapharyngeal, cervical, precapsular, prefemoral, and hepatic nodes as well as in the mesenteric nodes.

Fig. 10.9. Midsagittal section of a bovine uterine horn with tuberculous metritis. Acc. No. 3864.

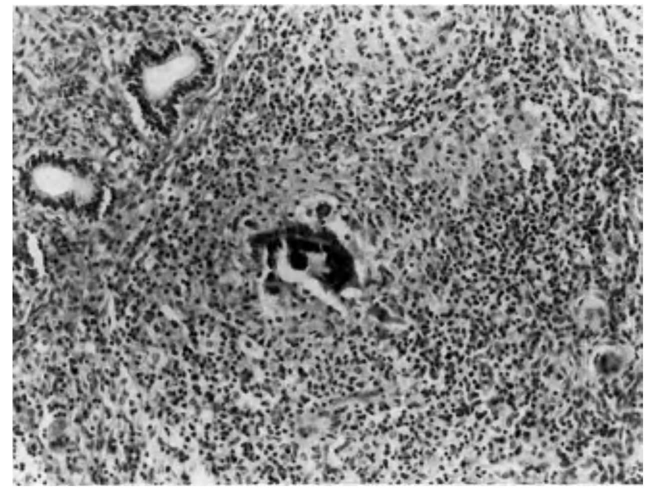

Fig. 10.10. Tuberculosis granuloma in the bovine endometrium. × 148. Acc. No. 687.

Plum (1938) reported that "in the period from 12/11/36 to 3/4/38, the State Veterinary Serum Laboratory received 17,697 placentae from aborting cows, and in 159 of these cases (i.e., 0.9%) the lesion was due to infection with tubercle bacilli." The tubercle bacilli were typed in 152 cases, and in 6 cases (3.95%), the placenta was infected with avian tubercle bacilli. "According to Danish law, every cow suffering from uterine tuberculosis is destroyed at once. . . . On autopsy of such animals some time after abortion, the uterus will as a rule show a few or several submucous abscesses. . . . In other cases the autopsy may reveal no macroscopic processes whatever" (Plum, 1938).

Ottosen (1944) reported a case of uterine tuberculosis in a cow that had aborted about 1 month before term. Tubercle bacilli were demonstrated in the placenta, and the cow was slaughtered 3 weeks after aborting. The surface of the endometrium "was diffusely thickened (about 1.5 mm) and very wrinkled; the folds could be straightened out only with difficulty" (Ottosen, 1944). The uterine tubes and ovaries appeared to be normal. The endometrial surface epithelium was detached in most areas, and the endometrium was greatly thickened. A zone of collagenous connective tissue containing lymphocytes, macrophages, and polymorphonuclear leukocytes was present beneath the luminal surface of the endometrium. "The deeper layers of the endometrium showed well-defined processes typical of tuberculous tissue with epitheloid and giant cells. Tuberculous granulomas were found also in the peritoneum, inguinal lymph nodes and the mammary gland" (Ottosen, 1944).

Fincher *et al.* (1954) described the uterine lesions of avian tuberculosis in a cow with paresis and a gray, vulvar discharge. A 1.5 × 5-cm caseopurulent granuloma was found in the uterine mucosa following slaughter. A pure culture of *M. avium* was isolated from the uterus. Fine brown granules were noted in the meninges of the spinal cord and brain after microscopic examination revealed the presence of diffuse tuberculous leptomeningitis. All the inflammatory lesions in the uterus were microscopic with the exception of one grossly visible granuloma. "While the microscopic lesions in the uterus were discrete, adjacent sections stained for acid-fast organisms contained an abundance of bacilli, which were scattered diffusely through the endometrium and myometrium. . . . Many acid-fast bacteria were seen, including large clumps, without any inflammation or necrosis in their vicinity" (Fincher *et al.*, 1954).

Tuberculosis of the uterus has been reported in swine and cats, is rare in dogs, and has not been reported in the horse (Innes, 1949; Jennings, 1949; Francis, 1958). Jennings found tuberculous metritis in three of five infected cats. One of the cats had a continuous vaginal discharge following parturition. Numerous acid-fast bacilli were present in the exudate. Jennings stated that "in the dog infection is largely via the respiratory tract, whereas in the cat it is almost invariably through the intestinal tract." It was stated that the dog may be infected with the human, bovine, and avian types of the tubercle bacillus while infection in the cat is invariably due to the bovine strain.

Vibriosis (Campylobacteriosis)

The organism that had been known as *Vibrio fetus* for about 50 years is now called *Campylobacter fetus. Campylobacter (Vibrio) fetus venerealis* is the cause of a specific venereal disease of cattle that is manifested by failure of conception, embryonic death, and abortion. The disease may be spread by infected bulls during natural service or by artificial insemination with semen to which antibiotics have not been added. It does not spread from cow to cow by contact (McEntee *et al.*, 1959). Most cows recover within a few months and develop a reasonable degree of immunity. Bulls do not develop clinical signs of the disease and do not become permanent carriers until they are at least 3 to 4 years old. The carrier state in the bull is associated with the development of epithelial crypts in the penile mucosa. The crypts are androgen-induced, become well developed at 3 to 4 years of age, become increasingly prominent with increased age, and provide a habitat for the organisms.

The early endometrial lesion in the infected cow consists of a neutrophilic infiltration of the zona compacta, surface epithelium, and the endometrial glands near the uterine lumen. This reaction is followed by a perivascular and periglandular infiltration of mononuclear cells consisting of lymphocytes, macrophages, plasma cells, and large mononuclear cells that are difficult to identify by light microscopy. Corbeil *et al.* (1975b) identified the large mononuclear cells ultrastructurally as lymphoblasts. Usually, bacteria are cleared from the uterus 40 to 60 days following infection, but they remain in the cervix and vagina for several additional months (Vandeplassche *et al.*, 1963). Endometritis subsides and fertility returns after the organisms are cleared from the uterus. The endometritis induced by *Campylobacter fetus venerealis* is nonspecific. Similar lesions occur during uterine infection with a variety of bacteria and *Tritrichomonas fetus*.

Campylobacter fetus fetus (intestinalis) and *Campylobacter fetus jejuni* inhabit the intestinal tract of cattle, sheep, and goats. *Campylobacter fetus fetus* causes enzootic abortion in sheep and sporadic abortion in cattle. *Campylobacter fetus jejuni* causes abortion in sheep and goats. The intestinal strains of *Campylobacter* infect the gravid uterus and placenta during periods of bacteremia. Schurig *et al.* (1973) injected a strain of *C. fetus fetus* of bovine fetal origin into the uterus, cervix, and cranial portions of the vagina of three heifers. Two of the heifers developed endometrial lesions similar to those induced by *C. fetus venerealis*.

Contagious Equine Metritis

Contagious equine metritis (CEM) is a highly contagious venereal disease of horses. The infection is due to a gram-negative, microaerophilic coccobacillus that has been provisionally named *Haemophilis equigenitalis* (Taylor *et al.*, 1978). The disease in mares is characterized by a mucopurulent vaginal discharge 2 to 10 days after breeding to an infected stallion (Hughes, 1978). The discharge persists for up to 3 weeks. In some mares, the only clinical sign of disease is a shortened estrous cycle. Stallions harbor the infection but do not have clinical signs of the disease.

Acland and Kenney (1983) described the lesions in 23 mares infected with the CEM organism by intrauterine inoculation. The mares were killed at intervals of 2 to 116 days following inoculation. The uterine tubes of one mare, killed after 35 days, were enlarged and contained a small quantity of viscid translucent fluid. "There was severe diffuse infiltration of the lamina propria by neutrophils, lymphocytes, macrophages and plasma cells. Large numbers of cells, mostly neutrophils, were present in the lumen. Fourteen of the other 22 mares had mild, subacute, usually bilateral salpingitis." White, translucent, odorless, viscid fluid was present in the uterus of mares killed 2 to 14 days postinoculation. The endometrial folds "were turgid and swollen and had a smooth glistening surface and gelatinous stroma." Small numbers of neutrophils were present in the stratum compactum and migrating through the surface epithelium at 2 days. At 8 and 11 days, numerous neutrophils, lymphocytes, macrophages, and plasma cells were present in the stratum compactum, and a few were present in the stratum spongiosa.

The inflammation was most severe at 14 days, and plasma cells were more numerous than neutrophils, lymphocytes, and macrophages. Neutrophils, within the uterine lumen, were most numerous at this time. "By 21 days the number of infiltrating and migrating cells had decreased, but the infiltrate still was diffuse and the cells still were predominantly plasmacytic. Neither erosion nor hyperplasia of the luminal, ductular or glandular epithelium was seen at any stage" (Acland and Kenney, 1983).

After 21 days, inflammation decreased but "persisted as a mild or multifocal lymphocytic endometritis to at least 116 days—the longest duration in our study." The lesions in the cervix were similar to those in the uterus but there was less edema. Inflammatory lesions were present in the vagina, vestibule, and vestibular glands. They concluded that "lesions caused by other pathogenic bacteria would be similar to those in contagious equine metritis and that there are not histologic diagnostic features for this disease."

Trichomoniasis

Trichomoniasis, due to *Tritrichomonas (Trichomonas) fetus*, is a venereal disease of cattle characterized by failure of conception, embryonic, death, pyometra, and abortion. According to Bartlett (1947b), "Early termination of pregnancy with early return to estrus and continuing catarrhal metritis is the most common consequence of trichomoniasis in the female." He also stated that "abortions of recognizable embryos and fetuses, pyometras and successful gestations despite infections are more likely to occur in cows experiencing reinfections—in herds where trichomoniasis has been present for several years."

Parsonson *et al.* (1976) investigated the pathogenesis and pathology of *Tritrichomonas fetus* infection in virgin heifers. Nineteen of 20 two-year-old heifers became infected after a single mating to an infected bull. Groups of two animals each were killed at approximately 2-week intervals after mating. They reported that "no macroscopic nor microscopic lesions were seen in the genital tracts or foetuses of the eight heifers killed before 50 days, although *T. foetus* was cultured from several areas of the genital tract in all animals." Five of the eight were pregnant at the time of necropsy. "In the nine heifers killed between 60 and 95 days after infection and from which *T. foetus* had been consistently cultured from CVM (cervicovaginal mucus) samples, two had impending abortions and five were not pregnant, one having pyometra. Seven had microscopic lesions ranging from a marked vaginitis, to generalized acute or chronic inflammation of the genital tract" (Parsonson *et al.*, 1976). Two cows had no reproductive tract lesion.

In two heifers that were pregnant at 60 and 95 days, *T. fetus* was present in the uterus and uterine tubes and in the fetal fluids and placentomes. Neutrophils and macrophages were present in the placentomes, and numerous trichomonads were demonstrated by the Gomori methenamine silver stain. The surface endometrium in the intercaruncular area was eroded, and numerous neutrophils and macrophages were present in the stratum compactum. These animals also had salpingitis and cervicitis. Three cows had chronic endometritis and salpingitis. Periglandular and perivascular foci of cells, composed mostly of lymphocytes with some macrophages and plasma cells, were present in the endometrium.

Fitzgerald *et al.* (1958) inoculated the reproductive tracts of 18 heifers with trichomonads isolated from the nose, stomach, or cecum of pigs. The infections lasted for 20 to 133 days. Three heifers that were bred artificially with a mixture of diluted semen and trichomonad cultures from swine failed to conceive. "A bull became infected with swine cecal trichomonads as a result of breeding an experimentally infected heifer; this bull then transmitted the infection to a virgin heifer by coitus. The bull remained positive for four months."

Schistosomiasis

Obwolo and Rogers (1988) reported the presence of schistosomal lesions in 43 of 3441 uteri from cows in Zimbabwe: "The lesions were inflammatory reactions associated with numerous schistosome eggs. Multinucleated giant cells occurred singly or formed complete rings around eggs or egg shells. In places, giant cells occurred around eosinophil abscesses which had presumably replaced destroyed eggs." The few adult schistosomes in the lesions were enclosed by fibrous tissue. The lesions were most severe in the uterine muscle. Obwolo and Rogers stated that "The report by Ferreira (1982) of schistosome lesions in the corpus luteum of 2 cows appears to be the only reference to the occurrence of such lesions in the genital tract. In the present study, examination of the genitalia was restricted to the uterine body and horns."

Amebiasis

Yasuda *et al.* (1988) reported the presence of numerous amebae (mostly trophozoites) in the uterus of an aged bitch with cystic endometrial hyperplasia and metritis. The bitch had a bloody vaginal discharge and ovarian follicular cysts.

Staphylococcal Infection

Fennestad *et al.* (1955) reported an outbreak of endometritis due to *Staphylococcus aureus* infection in sows bred to an infected boar. The boar had normal fertility for about 1 year. Only 4 of 18 sows conceived following service by the boar during the subsequent 3 months. "Eight sows developed symptoms of metritis in from 8 to 19 days after copulation; one sow died of metritis, the others apparently recovered after treatment with penicillin. Three, however, had a relapse of the disease from one to three months later." Two of the apparently recovered sows aborted following service to other boars, and *S. aureus* was isolated from the placentae and fetuses. The signs of metritis included elevated temperature (up to 41°C), purulent vulvar discharge, anorexia, apathy with an inclination to lie down, and a kyphotic gait.

The boar appeared to be clinically normal, and *S. aureus* was the predominant organism isolated from a preputial wash. Following slaughter, an abscess was found in the submucosa of the urinary bladder. *Staphylococcus aureus* was isolated from the abscess, vesicular glands, prostate, and urethra. Cultures from the testes, epididymides, and bulbourethral glands were negative.

The gross uterine lesions resembled those of brucella endometritis described by Thomsen (1934). Firm, white to yellow nodules, 1 to 5 mm in diameter, were present in the endometrium. A small quantity of gritty, gray-yellow exudate was present in the center of the nodules. The nodules consisted of central masses of gram-positive cocci surrounded by radiate, club formations of acid-fast hyaline material and purulent exudate. The exudate was surrounded by a narrow zone of granulation tissue "composed of polygonal epithelioid cells in a reticular arrangement, with oval nuclei with a low chromatin content, and a few polynuclear giant cells of irregular shape with marginal round nuclei with varying content of chromatin. The nodules were surrounded by a connective tissue capsule composed of collagen fibrils in concentric arrangement, most close-set peripherally" (Thomsen, 1934). Lymphocytes and plasma cells were present in the capsule. Histologically, the nodules resembled actinomycosis. Staphylococci also produce necrosing endometritis in swine.

Laing and Downe (1946) reported an outbreak of staphylococcal infection in 41 cows and 10 heifers following natural service to a single bull. A yellow-white vulvar discharge occurred following service, and many of the animals returned to estrus at about 3 weeks following service. Three cows aborted at 5 months. No lesions were found in the bull following slaughter. The fertility problem subsided following the vaccination of the cows with a staphylococcus toxoid.

Endometritis occurs occasionally in virgin heifers that are bred by nonvirgin bulls. These infections may be due to staphylococci, streptococci, or other bacteria harbored on the prepuce and penis of the bull. Infected heifers have a purulent vulvar discharge after mating and fail to conceive until endometritis resolves. Pluriparous cows develop immunity to a variety of bacteria carried by the bull and are less susceptible to a variety of infectious agents than virgin heifers.

Necrobacillosis

Fusiformis necrophorum infection of the uterus can be a fatal postpartum disease of cattle and sheep. It is often superimposed on traumatic or other lesions of the uterus. The lesions consist of dry coagulative foci of necrosis surrounded by a zone of hyperemia and inflammation. The uterine mucosa is thickened considerably and has ulcerated necrotic areas. Tangled masses of long filamentous organisms are present at the junction of the necrotic and inflammatory areas. Vasculitis with thrombosis is a characteristic feature of the disease.

Fungal Infections

The gravid uteri of ruminants are susceptible to fungal infections, but nongravid uteri are very resistant. The only case of mycotic infection that I have seen in a nonpregnant cow occurred in an area of the uterus that was traumatized during parturition. A lacerated area in the ventral uterine body had an area of necrosis containing hyphae of a mucoraceous fungus. The necrotic tissue was surrounded by granulation tissue.

"Excessive or prolonged intrauterine infusion of antibiotics in the treatment of chronic endometritis in mares is usually followed by the establishment of fungi and yeasts in the genital tract" (Zafracas, 1975). Twelve of 16 mares with *Candida* infection had pneumovagina even though a Caslick's operation to correct pneumovagina had been performed. *Candida albicans, C. parapsilosis, C. histiniae, C. rugosa,* and other *Candida* spp. were isolated from different cases. "Uterine biopsy was performed in eight of the infected mares and histological examination of the specimens showed various degrees of endometrial edema and round cell infiltration, especially around the endometrial glands and blood vessels" (Zafracas, 1975). The prognosis for future fertility is poor in mares with *Candida* infection.

Viral Infections

Many viruses are known to infect the pregnant uterus, but relatively little is known about their effects on the nongravid uterus because the reproductive organs are seldom examined in the case of systemic viral infections.

Canine Distemper. Invasion of the uterus by the distemper virus results in the formation of cytoplasmic and intranuclear inclusions, without inflammation, in sexually immature dogs. In adults, a small amount of purulent exudate may be discharged from the vulva as an early sign of the disease. The uterus contains a small amount of pale yellow exudate. The surface epithelium and the glands in the crypt zone contain numerous, round to irregular-shaped, acidophilic, cytoplasmic inclusions and a few oval to spherical intranuclear inclusions. The cytoplasmic inclusions may be so numerous and bizarre in shape that they resemble those in tissue culture inoculated with distemper virus. Numerous neutrophils are present in the stroma and in the lumina of the endometrial glands. Multifocal areas of necrosis are present in the glandular epithelium. The inflammatory reaction extends into the intermediate zone in fingerlike projections along the glands. The intermediate zone is edematous. The basal zone is usually free of inflammation and inclusion bodies.

Bovine Herpesvirus Infection (Infectious Bovine Rhinotracheitis, IBR). Kendrick and McEntee (1967) reported the effects of inseminating 12 heifers with 1 ml of semen mixed with 1 ml of IBR virus suspension. Endometrial biopsy specimens were obtained from 8 heifers on the 2nd, 3rd, and 4th days and at approximately 14 days postinoculation.

Nine of the 12 heifers returned to estrus within 9 to 13 days following breeding and inoculation. Intranuclear inclusions were present in the epithelial cells of the surface epithelium at 48 hours. The nuclei of affected cells were enlarged and filled with a homogeneous or finely granulated blue to blue-red material, and the chromatin was marginated. Although it was not mentioned in the report, intranuclear inclusions were also present in stromal cells adjacent to the affected surface epithelium. Neutrophils were present immediately below the degenerating epithelium, and the tunica propria was edematous. Inclusions were not found at 72 hours after inoculation. Necrosis of the surface epithelium was extensive and had spread into the connective tissue in the superficial portion of the zona compacta. Numerous neutrophils were present in the zona compacta, and the zona spongiosa was edematous. By the fourth day necrosis had extended deep into the endometrium, and numerous neutrophils and macrophages were present in the necrotic tissue and in the uterine lumen. On Days 11 to 15 postinoculation, the surface epithelium was absent in a few areas and regenerating in other areas. Neutrophils were migrating through the epithelium and subepithelial hemorrhage and edema were present. Many lymphocytes were scattered throughout the endometrium and a few small lymphocytic foci were present. All animals with cycles of 15 days or less had endometritis.

White and Snowdon (1973) reported the results of breeding cattle with semen naturally contaminated with IBR virus, from a bull in a commercial artificial breeding center. The breeding records of 20 herds, in which the contaminated semen was used, were studied. The fertility of the bull that had shed virus was compared to that of other bulls used in the same herds. They reported that "semen collected from bull A, and which contained in excess of 10^6 $TCID_{50}$ of IBR virus per ml, was distributed from a commercial artificial breeding center. The semen produced a non-return rate of 13.4% when used to inseminate cows in 20 herds. Cows in the same herds, but inseminated with semen collected from other bulls, had a non-return rate of 60.8%." Apparently, the contamination of the semen was not entirely responsible for the low fertility, because cows bred to this bull during the year before contamination of the semen had a low non-return rate (33.7%). "Of the cows that returned to service after insemination with contaminated semen from bull A, there was a significant number (22.1%) with shortened oestrous cycles, that is less than 18 days" (White and Snowdon, 1973).

Lomba *et al.* (1976) reported the occurrence of metritis, due to IBR infection, 3 to 7 days following cesarean section. They reported that "There was a sudden onset of the disease with severe signs, including hyperthermia (41°C to 42°C), anorexia and painful hyperaemia of the vulva and vaginal mucosa. . . . The uterus was voluminous and flaccid, filled with abundant reddish, practically odourless exudate and containing debris of cotyledons and the uterine mucosa. . . . Large necrotic foci appeared in the vaginal mucosa. . . . Upon rectal palpation of the uterus, a pathognomic crepitation was perceived." Only a brief mention was made of the postmortem findings, which included an acute and subacute endometritis with necrosis of the epithelium. IBR virus was isolated from the uterine exudate. The disease was observed only in cows having undergone a cesarean section. They stated that "the question arose whether the virus was spread by the veterinary surgeon or whether it was already present and developed after the stress of the surgical procedure. . . . Correct surgical procedures, using carefully cleaned and sterilized clothes, gloves and instruments proved to be very effective in preventing the disease."

Endometrial Necrosis

Chemical Irritants

Intrauterine infusion of iodine solutions, nitrofurazone, and oxytetracycline may shorten or lengthen the bovine estrous cycle (Nakahara *et al.*, 1971a,b; Grunert *et al.*, 1973; Seguin *et al.*, 1974; Ginther and Meckley, 1972; Oxender and Seguin, 1976). Infusion of these preparations early in the estrous cycle (Days 3 to 9) results in an early return to estrus, whereas infusion on Days 14 to 17 causes a delay in the return to estrus. Infusion during mid-diestrus or near estrus does not alter the cycle length. The preparations cause necrosis of the surface epithelium and necrosis, hyperemia, and edema of the zona compacta. The damaged endometrium regenerates within a few days.

Kopljar (1964) investigated the effects in cattle of intrauterine infusions of Lugol's solution, lotagen, aureomycin, streptomycin, embryostate, and stilbestrol. Lugol's solution produced the most severe uterine lesions, lotagen and aureomycin induced less severe damage, and embryostate caused mild changes. No changes in the endometrium were noted following infusions of streptomycin and stilbestrol.

Viral Infection

The necrotizing effect of infusing the bovine uterus with IBR virus is described in the preceding section on viral infections of the uterus.

Traumatic Lesions

The bovine uterus can be injured by the improper use of insemination pipettes, uterine catheters, and biopsy punches. If the trauma is limited to the endometrium, usually it will heal rapidly without adverse effects. If the uterus is perforated in cows with endometritis, parametritis and adhesions may develop.

Uterine Lacerations during Parturition

Laceration of the endometrium occurs occasionally in heifers during their first parturition. The most common lesion is located in the ventral part of the uterine body and usually extends into the cranial part of the cervix. The separation of the endometrium extends to the myometrium. Most of the lesions heal uneventfully and leave a scar covered by a single layer of epithelial cells. Uterine glands do not regenerate in the scar tissue. Rare complications include the development of mycotic granulomas, fatal hemorrhage, or the formation of soft, brown calculi in the depressed area of the scar. The calculi are composed mostly of blood from metestrous bleeding. The only case of a mycotic granuloma that I have seen in a nongravid bovine uterus occurred in a ventral laceration of the uterine body and caudoventral portion of one uterine horn in a 3-week postpartum cow. The edges of the lacerated area were markedly thickened and hemorrhagic and protruded into the uterine lumen. The tissue was necrotic, infiltrated by neutrophils, covered by fibrin, and surrounded by proliferating fibrous tissue. Large, irregular-shaped, branching hyphae infiltrated the necrotic tissue.

A 10-year-old Holstein cow was slaughtered 16 days postpartum because of massive uterine hemorrhage into the peritoneal cavity. Numerous blood clots were discharged from the vulva immediately after calving. The placenta was expelled normally and the cow ate well but milk production was slow to return to normal. The cow acted uneasy during the morning of Day 16 postpartum. At 3:00 P.M. she started to pass free and clotted blood from the vulva. The cow was slaughtered 5 hours later because it appeared that she was bleeding to death. A 25-cm rupture was present in the dorsal part of the previously gravid horn, about 11 cm cranial to the cervix. A 15-cm laceration was present in the uterine body and ventral portion of the same horn. The broad ligament on that side was very edematous. It appeared that the ventral uterine laceration occurred during calving and caused early postpartum hemorrhage. The continued bleeding distended the uterus, which ruptured dorsally on the day of slaughter.

Complications of Ovariohysterectomy

Pearson (1973) discussed the complications of ovariohysterectomy in the bitch. They include hemorrhage, adverse tissue response to ligature material, recurrent estrus when some ovarian tissue is left in the abdomen, pyometra when uterine tissue is not completely removed, intestinal and peritoneal adhesions, urinary incontinence, infantile vulva in bitches spayed before puberty, and peritonitis due to perforation of the uterine wall during surgery in cases of pyometra. The latter condition may occur easily when the bitch has adenomyosis in addition to pyometra.

Acquired Changes in Position

Uterine Torsion

Torsion of the uterus occurs most frequently in cattle and occasionally in the other species of domestic mammals. Roberts (1971) stated that "in the cow, sheep and goat, the gravid horn is in the shape of an arc or 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, as illustrated by Benesch, when one horn rotates out its base. A modification of this same volvulus type of torsion occurs when only a portion of one horn, containing usually one fetus, may be twisted or rotated. In unipara . . . both gravid and non-gravid horns are involved in the torsion."

Cow. Uterine torsion is a common cause of dystocia in cattle with a frequency ranging from 5 to 27% of the cases of dystocia. In a series of 133 cases, which were selected for surgery, the degree of torsion varied from 90° to 1080° with 360° torsions being the most numerous (Pearson, 1971). Pearson stated that "As these were selected cases referred for surgery, these figures may not be representative of the degree of rotation in unselected cases of torsion." According to Wright (1958), "the degree of twist varies from 90° to 180°, the latter being more common in cows than heifers." Torsions of the bovine uterus are anticlockwise in the majority of cases and the cranial vagina is usually involved. Most cases occur during parturition.

In regard to etiology of the condition, Wright stated that "It cannot be doubted that the disposition of the heavily gravid uterine cornu and the site of attachment of the broad ligament predispose to torsion, but it is the exciting cause which arouses greater interest. It would seem to me almost certain that the condition occurs during the first stage of labour, at the time the cervix is dilating prior to the expulsive second stage, for it is inconceivable that the cervix would undergo any dilatation if a 180° twist had occurred at the uterine isthmus prior to the onset of natural dilatation. Moreover, the first stage is associated with particularly vigorous calf movement."

Sow. Pearson (1971) reported five cases of uterine torsion in swine: "In all the sows, the torsion was precervical affecting the uterine body in two animals and the lower part of one horn in the remaining three. All sows were parturient."

Mare. Skjerven (1965) reviewed 11 cases of uterine torsion in the mare: "All of the mares had shown symptoms of colic for a period of from one to several days, and exhibited varying degrees of malaise." Nine of the 11 torsions occurred before term with 5 occurring to the right and 6 to the left. The degree of torsion varied from 180° to 540°.

According to Vandeplassche *et al.* (1972), 5 to 10% of all serious dystocias in the mare are due to uterine torsion. They reported that "More than half the cases occur before the end of gestation and in the majority, the uterus turns through a full 360° or more. Twisting in an anti-clockwise direction occurs more frequently than twisting in a clockwise direction. Left torsions prevail and as yet no satisfactory explanation to account for this apparent directional preference has been advanced." In a series of 42 treated mares, 40% of the mares and 71% of the foals died. The causes of death of the mares were uterine rupture, shock, torsion of the colon, and hemorrhage. Torsion of the colon may have been due to rolling associated with the pain induced by the uterine torsion or vice versa.

Bitch and Queen. Uterine torsion is comparatively rare in the bitch and queen and usually involves one uterine horn but occasionally both. It occurs most often in pregnant animals at or near the time of parturition. Torsion may occur in nonpregnant dogs with pyometra (Bloom, 1954) and pseudopregnancy (Rendano *et al.*, 1974) and in dogs and cats with endometrial polyps. Bloom reported that "The torsion may be either to the right or left and varies in degree from a slight twist to one or two complete twists, and the broad ligament is commonly ruptured or torn. In a complete twist, the uterine horn may be torn or even completely separated from the uterus at the point of torsion."

The sequelae of uterine torsion in the dog and cat depend on the degree of torsion and include death of the fetuses, shock-induced death of the mother, necrosis and rupture of the uterus, complete separation of the uterus in one horn or in the uterine body, perforation of the broad ligaments, peritonitis, and adhesions between the uterus and omentum and/or abdominal wall.

Uterine Prolapse

Vandeplassche and Spincemaille (1963) stated "It appears that this puerperal trouble occurs more frequently in sheep than in cattle. The frequency in sows is lower than in cows. Prolapse of the vagina, forced extraction of the fetus, puerperal paresis and hypotonia uteri definitely act as predisposing factors for uterine prolapse." They found that the prolapse starts in the uterine body rather than in the cranial portions of the uterine horns. Uterine prolapse is rare in the mare, bitch, and queen.

Cow. Odegaard (1977) conducted a clinical study concerning the incidence, recovery, and subsequent fertility of 955 cows with uterine prolapse. Twenty-seven percent of the prolapses occurred within 1 hour after parturition, 48% within 3 hours, and 90%

within 15 hours. The latest time of occurrence was 51/2 days postpartum. "There was a highly significant correlation between plasma calcium level and the time of occurrence ($P > 0.001$). For each 1 mg/100 ml fall in plasma calcium, there was an increase of 0.8 hours in the time interval between parturition and time of occurrence" (Odegaard, 1977). He concluded that hypocalcemia predisposes to uterine prolapse by delaying involution of the cervix.

In regard to the occurrence of prolapse in different age groups, it was stated that "even though the heifers were numerically the largest group, the incidence of uterine prolapse in cows with five or more calvings was three times as high as in heifers or second calvers. However, the conclusion cannot immediately be drawn that old age is a disposing factor. The incidence of hypocalcaemic parturient paresis in cows with uterine prolapse was far higher than the estimated incidence for the individual calving numbers in a Norwegian cow population" (Odegaard, 1977). When cows that had uterine prolapse but did not have hypocalcemia were compared with the control population, there was no significant difference in age distribution. Also, a comparison between cows with prolapse and controls with hypocalcemic parturient paresis did not reveal a significant difference in age distribution between these groups. It was stated that "complicated birth was significantly more common in heifers with uterine prolapse than in older cows."

Seventeen percent of the affected cows failed to recover. About 25% of the "non-recovered" cows were slaughtered because of uterine injury or an irreplaceable prolapse. Rupture of blood vessels was diagnosed in seven cows that died before or during treatment. "Mortality was five times as high in prolapse cows with hypocalcaemic parturient paresis as compared with control cows with hypocalcaemic parturient paresis, and about twice as high as in prolapse cows without hypocalcaemic parturient paresis" (Odegaard, 1977).

Approximately 65% of the cows were culled with about one-third being eliminated because of fear of recurrence of uterine prolapse. About 44% were culled without being bred. Of the cows bred, 11.6% were discarded with infertility as the sole reason and 7.1% because of failure to conceive combined with other reasons.

Ewe. Relatively little has been published on uterine prolapse in sheep. In regard to ewes grazing on subterranean clover pastures in Australia, Bennetts *et al.* (1946) reported that "The problem has these manifestations: infertility, dystocia and a prolapse of the uterus which generally occurs some months after parturition and which may affect even unbred animals." The phytoestrogens—genistein, biochanin A, and formononetin—are present in clover pastures (Beck, 1964).

Herniation of the Uterus

Ventral herniation of the gravid uterus through a rupture of the abdominal wall occurs occasionally during advanced pregnancy in the cow, ewe, goat, and mare (Arthur, 1975). The gravid and nongravid uterine horns of the dog and cat may be involved in inguinal hernias (Short, 1963). Bellenger *et al.* (1975) reported herniation of the gravid canine uterus into the thoracic cavity.

Rupture of the Gravid Uterus

Rupture of the gravid uterus occurs in all species of domestic mammals and may occur spontaneously or may result from faulty obstetrical technique. Spontaneous ruptures usually occur during late gestation or during parturition.

Cow

Hopkins and Amor (1964) reviewed the literature on rupture of the gravid bovine uterus. Most ruptures occur during obstetrical manipulations. Spontaneous ruptures may occur as the result of torsion of the uterus, prolonged labor in cases of breech presentations, or a fall.

Bitch and Queen

Uterine torsion in the dog and cat usually involves one uterine horn and sometimes results in rupture of the torsed horn, thereby allowing the enclosed fetuses to drop into the peritoneal cavity. The fetuses may become mummified or macerated. There are reports of true (primary) extrauterine (ectopic) pregnancies in dogs and cats, but none of the reports is adequately documented to substantiate the claims.

I examined the reproductive tract from a 2 1/2-year-old German Shepherd bitch that had whelped three normal pups 4 months prior to routine ovariohysterectomy. The right uterine horn was completely separated in the midportion (Fig. 10.11). Omentum was firmly attached to the detached cranial portion of the horn. Numerous oval-shaped nodules of cartilage were present in the broad ligaments and in the omentum. Although the clinician did not have a record of any unusual clinical signs during or following parturition, it appears that the bitch had uterine torsion resulting in separation of the right uterine horn. Apparently escaped uterine content induced cartilagenous metaplasia in the omentum and broad liga-

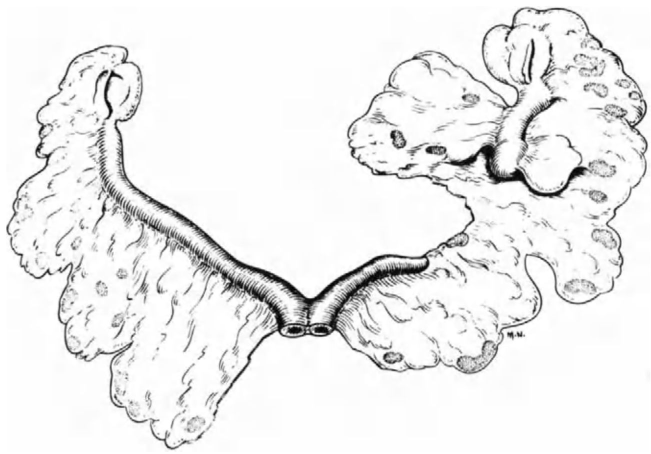

Fig. 10.11. Complete separation of the right uterine horn of a bitch. Nodules of cartilage (stippled areas) are present in broad ligaments. Acc. No. 12063.

ments. Mummified fetuses or fetal bones should have been present in the abdominal cavity, but they were not searched for during surgery.

Postpartum Lesions

Subinvolution of Placental Sites

Beck and McEntee (1966) reported a case of subinvolution of the placental sites in a 2-year-old bitch that had a blood-tinged vulvar discharge for 2 months following whelping. A variety of treatments failed to correct the condition so the bitch was ovariohysterectomized. The former implantation sites were about twice normal size (Fig. 10.12), and a small amount of blood-tinged fluid was present in the uterine lumen.

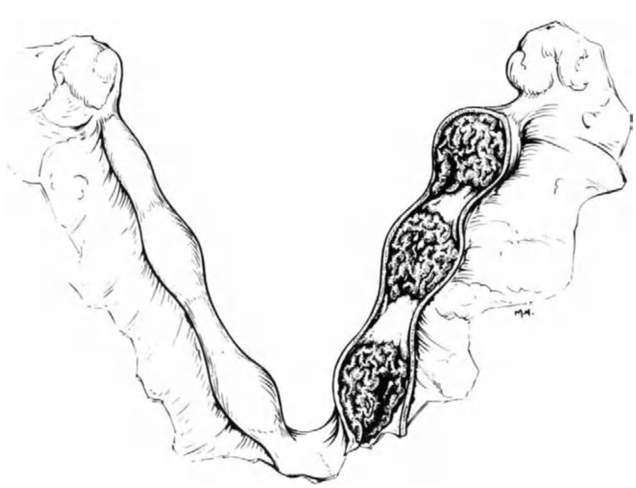

Fig. 10.12. Subinvolution of placental sites in a 68-day postpartum bitch. Acc. No. 7984. (Beck and McEntee, 1966.)

The enlarged areas of the endometrium were roughened, were gray to brown, and contained hemorrhagic areas (Fig. 10.13). "Histologic examination revealed the presence of large masses of eosinophilic, slightly granular material in the enlarged areas of endometrium. Endometrial glands and blood vessels penetrated the peripheral areas of the eosinophilic masses. There were multiple hemorrhages of varying size and numerous hemosidern-laden macrophages in the adjacent stromal tissue. Many cells with large nuclei and abundant vacuolated cytoplasm were present in the affected areas." (Beck and McEntee, 1966).

Other possible cases of this condition were reported by Riser (1940) and Nye (1950). The history and gross lesions of the case described by Riser as a chorioepithelioma are identical to those of subinvolution of placental sites. Only a brief description of the histologic lesions was presented. Nye reported a case of necrosis of the implantation sites in a 2-year-old bitch that had given birth to eight normal puppies between 4:00 A.M. and 4:00 P.M. By 9:00 P.M. on the following day, the bitch was in a collapsed state and showing abdominal pain and was hysterectomized 2 hours later. "On the side of the uterine horns there were found eight elliptical areas of necrosis, 1 inch by 1 1/2 inch in area, two of which were ruptured, the remaining being clearly visible from the serosal surface of the uterus. Each one was situated at the site

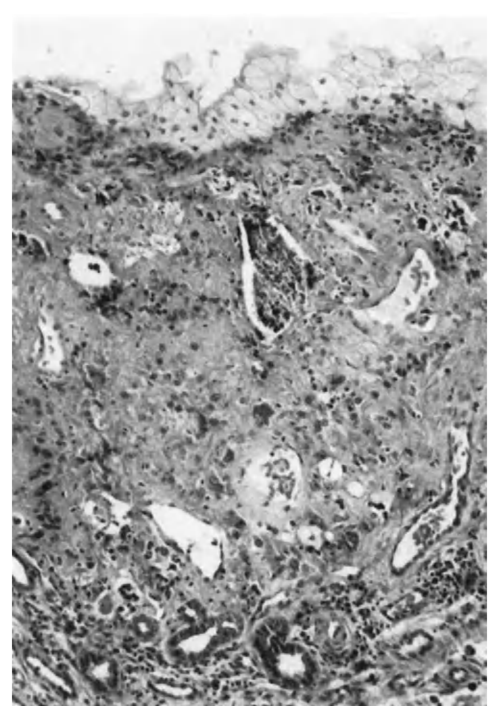

Fig. 10.13. Subinvolution of a canine placental site. × 100. Acc. No. 7984.

of placental attachment, yet no placental material remained in the uterus" (Nye, 1950). The bitch made an uneventful recovery. The uterus was not examined histologically.

Glenn (1968) described the clinical and pathologic features of subinvolution of placental sites in 32 postpartum bitches. Eighteen of 26 bitches, with available clinical histories, had a persistent postparturient, blood-tinged vaginal discharge. "The owners reported that they frequently observed bloody spots on the floor where the bitch had been sitting. The vaginal discharge persisted in 17 of these animals until ovariohysterectomy was performed six to 12 weeks postpartum." The animals with more severe hemorrhage had a mild to moderate anemia. Approximately two-thirds of the cases occurred in bitches under 3 years of age. Most had whelped normal pups.

Al-Bassam *et al.* (1981) diagnosed 20 cases of subinvolution of the placental sites in a series of 95 reproductive tracts from postpartum bitches. The diagnoses were based on a history of a persistent, bloody, vaginal discharge and on gross and histologic examination of the placental sites. "On gross examination, affected placental sites appeared from the serosal surface as large ellipsoidal swellings; the diameter of the largest was about twice the size of a normal site from the same breed at the same stage. The lumen of the uterus contained a small amount of blood-tinged fluid and the placental sites were irregularly thick, rough and gray to brown, with areas of hemorrhage of various sizes."

The most characteristic histologic feature of the condition is the presence in the endometrium of syncytial masses of cells with closely packed, vesiculate nuclei and abundant foamy to markedly vacuolated, pale, eosinophilic cytoplasm. These cells resemble syncytial trophoblasts but their identity has not been established. The syncytial cells invade the myometrium and perforate the serosa in some cases. Because of their invasive properties, it appears that they are trophoblast rather than decidual cells. Masses of collagen and necrotic and hemorrhagic tissue protrude into the uterine lumen. Foci of mineralization are often present in the necrotic tissue. The surface epithelium covering the collagen is intact in some areas and denuded in others. Dense infiltration of lymphocytes, plasma cells, and macrophages surrounds the masses of trophoblast-like cells in some cases. The lesion appears to commence prior to parturition. I examined an affected canine uterus that ruptured during advanced pregnancy and allowed fetuses to drop into the peritoneal cavity. Extension of the lesion through the myometrium occasionally results in perforation of the postpartum uterus.

Arbeiter (1975) reported the unsuccessful use of the following treatments: oral administration of hemostatic compounds, parenteral use of compounds to increase uterine tone, uterine curettage, and uterine lavage with a chlorhexidine solution during laparotomy. Burke (1977) stated that "purified oxytocic principle (POP) or ergot alkaloids are of no value in the treatment of this disease." The majority of affected bitches probably recover spontaneously. However, those that do not recover can be ovariohysterectomized or treated with a progestational agent. Arbeiter treated the condition successfully with medroxyprogesterone acetate (MA): "Ten cases of persistent postpartum uterine hemorrhage in the bitch were treated with a single subcutaneous dose of 25 to 50 MA suspension (2 mg/kg body weight). Hemorrhage subsided within 24 hours, changed to a blood-tinged mucous vaginal discharge on Day 2 and disappeared on Day 3." Four bitches that were bred on the next heat after treatment conceived and had a normal gestation, parturition, and puerperium.

Serosal Inclusion Cysts

Serosal inclusion cysts of the uterus develop during postpartum uterine involution. The contraction of the myometrium causes infolding of the serosa. Portions of the peritoneum become embedded in the underlying connective tissue and form cysts.

Serosal inclusion cysts are found predominantly in

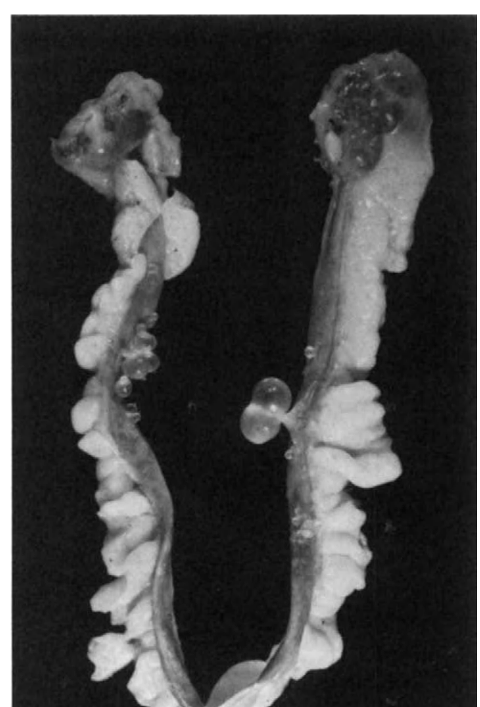

Fig. 10.14. Multiple serosal cysts on a canine uterus. Acc. No. 16036.

the aged multiparous bitch. The cysts are thin-walled, contain clear fluid, are up to 1.5 cm in diameter, and are located on the antimesometrial side of the uterus (Fig. 10.14). A few serosal inclusion cysts have been found in the cow and are usually located on the dorsal intercornual ligament.

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Chapter 11

The Uterus: Atrophic, Metaplastic, and Proliferative Lesions

Atrophy
- Cow
- Mare

Cysts
- Endometrium
- Myometrium
- Serosa

Squamous Metaplasia

Hydrometra and Mucometra
- Cow
- Ewe and Doe (Goat)
- Gilt
- Mare
- Bitch and Queen

Adenomyosis

Endometrial Hyperplasia
- Bitch
- Queen
- Cow
- Ewe
- Sow and Mare

Hyperplasia of the Uterine Serosa

Neoplasia
- Epithelial Tumors
- Mesenchymal Tumors

Bibliography

Atrophy

Atrophy of the uterus occurs in association with chronic debilitating diseases and following ovariectomy. Senile atrophy of the endometrium is not as important in domestic mammals as it is in women because animals usually retain reproductive function throughout life.

Cow

During periods of nutritional deficiencies, the ovaries of zebu cattle become smooth and nonfunctional, and the uterus atrophies. The inactive ovaries have a smooth surface and are devoid of corpora lutea and grossly visible follicles. When nutrition improves and ovarian function returns, the uterus returns to normal and the animals regain fertility.

Cows with mucometra, secondary to cystic follicles, have atrophy of the uterus superimposed on an earlier endometrial hyperplasia. The endometrium and myometrium become very thin. The endometrial glands remain cystic, but the glandular epithelium atrophies. The atrophic myometrial cells are composed predominantly of nuclei with only a small amount of deeply acidophilic sarcoplasm.

Mare

Knudsen (1964) reported uterine dilation, due to atrophy of the endometrium of the uterine body, in 40 mares that were 9 to 24 years of age. Some had been mistakenly diagnosed as pregnant. On clinical examination, the uteri were found to be asymmetrical with dilation of only one-half of the uterine body. At postmortem examination it was found that the mucosa of the affected portion of the uterus was flattened while the rest of the uterus appeared normal. The abnormal endometrium "was aglandular and covered by low cuboidal epithelium. Toward the transition to normal endometrium, could be found rudimentary glands lined by a simple squamous epithelium. The endometrium of the rest of the uterus contained normal or possibly even hypertrophied glands and was covered by a cylindrical epithelium" (Knudsen, 1964). The uterus contained exudate in some cases and mucus in others. The affected mares had poor fertility that was "ascribed to the acute endometritis which regularly appears within a few days after breeding, and which, in turn, depends upon the lowered resistance of the endometrium in the dilated regions."

Cysts

Endometrium

Cystic endometrial glands cannot be congenital because glands are not present at birth. As a result, all cystic endometrial glands can be attributed to acquired causes such as infection, accumulation of mucus in the uterus, postpartum involution of the uterus, and hormonally induced cystic hyperplasia.

Endometrial glands may become occluded and cystic because of severe endometritis. When the inflammation subsides, the dilated glands are lined by flattened epithelium and surrounded by fibrous tissue. The cysts remain indefinitely and provide evidence of previous infection.

Blockage of the cervical canal due to either congenital or acquired lesions results in the accumulation of secretory material in the uterine lumen and distention of endometrial glands. Andersen and Simpson (1973) reported the presence of multiple cysts, up to 2 mm in diameter, in the endometrium of 8 (14%) of 59 aged Beagle bitches. They stated that the cysts were not associated with endometrial hyperplasia, but they did not establish their pathogenesis.

Pericaruncular cysts (Fig. 11.1) develop occasionally in the ewe during involution of the uterus. The cases that I have seen were in ewes that had lambed several times. The flattening of the caruncles during the early stage of uterine involution compresses and occludes the lumen of some of the pericaruncular uterine glands and results in the development of cysts. These cysts do not appear to interfere with fertility.

Cystic endometrial hyperplasia occurs in the uterus of the cow, ewe, and bitch in association with hyperestrogenism. Progesterone induces a histologically different type of cystic endometrial hyperplasia in both the bitch and queen. The etiology of cystic endometrial hyperplasia in the mare and sow has not been determined. These conditions are discussed under the section "Endometrial Hyperplasia."

Fig. 11.1. Pericaruncular cysts in an 8-year-old ewe 6 hours postpartum. Acc. No. 7927.

Focal areas of lymphangiectasia occur in the endometrium of some mares that are over 10 years old. The pathogenesis of the lesion has not been established. Kenney and Ganjam (1975) reported that lymphangiectasia (lymphatic lacunae) has been found in "uteri containing endometrial cups and no conceptus and also in subfertile mares. Thus, they appear to interfere with the ability of a mare to become pregnant and may also be a cause of abortion."

Lymphangiectasia also occurs in the endometrium of aged sows. The lesions are usually multiple and bilateral. The dilated lymphatics are elongated, protrude into the uterine lumen, and may be several centimeters long. Histologic examination is often necessary to differentiate these lesions from cystic endometrial glands.

Myometrium

Focal areas of lymphangiectasia in the myometrium occur predominantly in the aged mare but have also been observed in the bitch and the cow. The lesions may be single or multiple. They may be present in any location in the equine uterus, but the largest and most frequent lesions are usually found in the ventral part of the uterine body. Lesions in the uterine body protrude ventrally and may be confused on clinical examination with an early pregnancy.

Segments of the mesonephric duct persist in the myometrium and in the broad ligament adjacent to the uterus in all species of domestic mammals. These persistent remnants tend to become cystic in aged animals. Prominent cystic mesonephric ducts are seen most often in the bitch and may be single or multiple, ranging in size from a few millimeters to several centimeters in diameter. The mesonephric remnants are surrounded by a prominent inner circular layer and a thin outer longitudinal layer of smooth muscle fibers. Sometimes the layers of muscle are intertwined. Estrogen stimulation, as seen in animals with cystic follicular degeneration, causes squamous metaplasia of the duct epithelium.

Serosa

Serosal inclusion cysts occur predominantly in the aged multiparous bitch and are described in Chapter 10.

Squamous Metaplasia

Squamous metaplasia of the endometrium is associated with highly chlorinated naphthalene poisoning in sheep but not in cattle (McEntee and Olafson, 1953). The metaplasia begins in the surface epithelium and gradually progresses to the depth of the glands. The uterine horns of affected animals become enlarged and firm. On gross examination of advanced lesions, it appears that the endometrium is covered by hair (Fig. 11.2). This appearance is due to the presence of plugs of keratinized epithelium protruding from endometrial glands.

The mycotoxin zearalenone induces edema and multifocal squamous metaplasia of the endometrium in swine. Chang *et al.* (1979) reported that "concentrations of 25, 50 or 100 ppm of 95% purified zearalenone fed to groups of healthy, multiparous sows during preestrus or throughout the gestation period (or both) produced multiple reproductive deficiencies. These reproductive disorders included infertility, constant estrus, pseudopregnancy, diminished fertility, reduced litter size, smaller offspring, malformation, juvenile hyperestrogenism and probably fetal resorption." In addition to squamous metaplasia of the uterus they found metaplasia in the uterine tube, cervix, vagina, and mammary gland.

Squamous metaplasia of the uterine surface epithelium occurs in some cases of postpartum pyometra in the cow, in association with prolonged cystic ovarian follicles in the cow, and in cystic hyperplasia–pyometra complex in the bitch. I have seen keratinizing squamous metaplasia of the endometrial surface epithelium in bitches that had received sialastic implants of estradiol during pregnancy. The bitches resorbed their fetuses and developed chronic endometritis. The endometrial glands were markedly dilated and lined by cuboidal epithelium. The metaplasia of the lining epithelium was much more severe than that present in naturally occurring cases of the cystic hyperplasia–pyometra complex or postpartum pyometra.

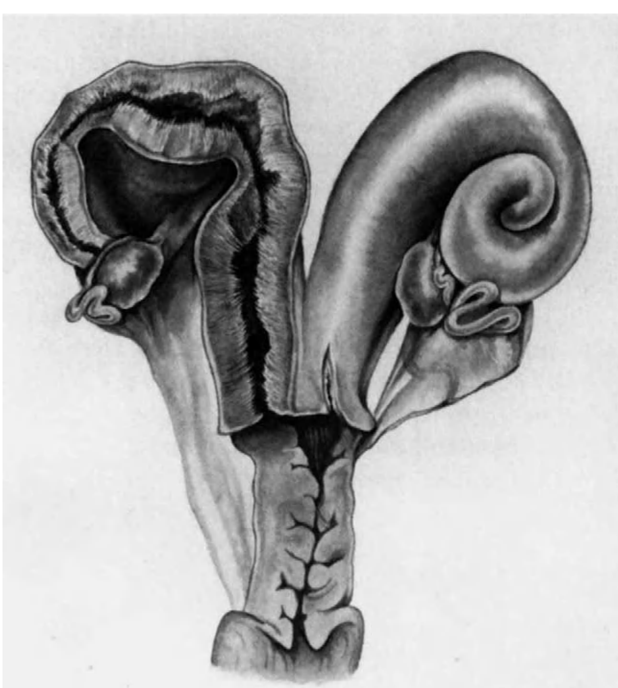

Fig. 11.2. Squamous metaplasia of ovine uterus due to highly chlorinated naphthalene poisoning. Hairlike plugs of keratin project into the uterine lumen. Acc. No. 676. (From McEntee and Olafson, 1953. Reproduced with permission of the publisher, The American Fertility Society.)

Hydrometra and Mucometra

Hydrometra is an accumulation of watery fluid, and mucometra is an accumulation of mucinous fluid in the uterine lumen. The main recognized causes of these conditions are congenital malformations of the cervix and uterus and hormonally induced cystic hyperplasia of the endometrium.

Cow

The congenital malformations of the cervix that result in the development of mucometra in the cow are discussed in Chapter 12. An accumulation of pale gray mucus is present in the uterus of some newborn calves.

An occasional parous cow, without an obvious cervical lesion, develops mucometra and remains in anestrum. Roberts and Fox (1968) reported a case of mucometra in a 3 1/2-year-old Holstein cow that had calved normally, was bred twice, and then failed to cycle. Fluid was detected in the uterus and a large corpus luteum was present in the right ovary about 5 months after the last service. The corpus luteum persisted, and the volume of uterine fluid varied from about 300 to 1250 ml until 7 months after the last breeding. The corpus luteum was "enucleated with great difficulty" and the cow came into estrum 4 days later. The cow was bred during the next estrus and conceived. They also reported a similar case found at an abattoir.

I have seen six cases of mucometra in cows with persistent corpora lutea and no obvious cervical defects. The uterine content consisted of amber to brown, watery to thick mucoid material that ranged in volume from 25 to 1400 ml. The smallest volume of content was found in the uterus of a 5-year-old cow that had not been in estrus for 3 months. The endometrium became thinner as the volume of uterine fluid increased. Periglandular fibrosis was present in the uteri with large volumes of mucoid material. The endometrial glands were dilated in most of the affected uteri.

I have examined the uteri from 14 cows with mucometra secondary to cystic follicular degeneration

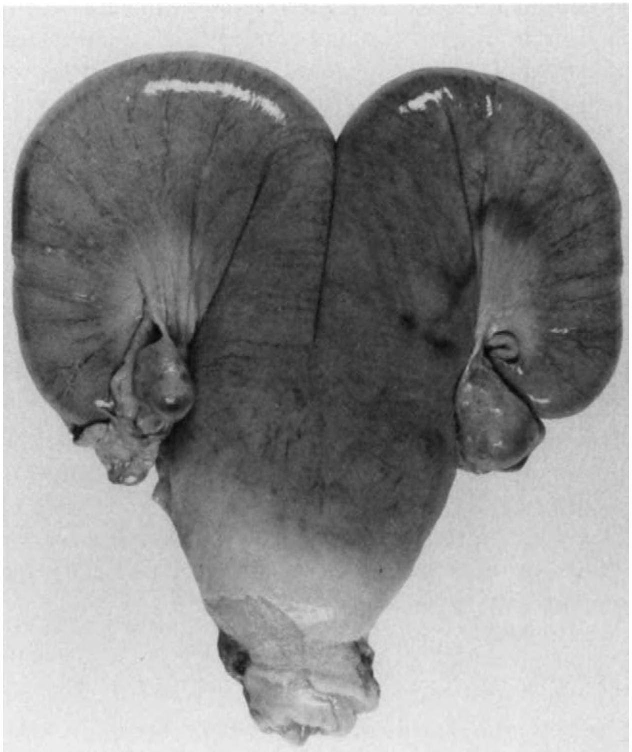

Fig. 11.3. Bovine reproductive tract with bilateral follicular cysts and 2.4 liters of cloudy, moderately tenacious fluid in uterine lumen. Acc. No. 4432.

(Figs. 11.3 and 11.4). Some of the cows showed signs of nymphomania until the time of slaughter while others were anestrus. The uterine content usually consisted of watery to slightly tenacious, gray, mucoid material. The volume of fluid ranged from 250 to 4800 ml. The microscopic lesions are described in this chapter under "Endometrial Hyperplasia."

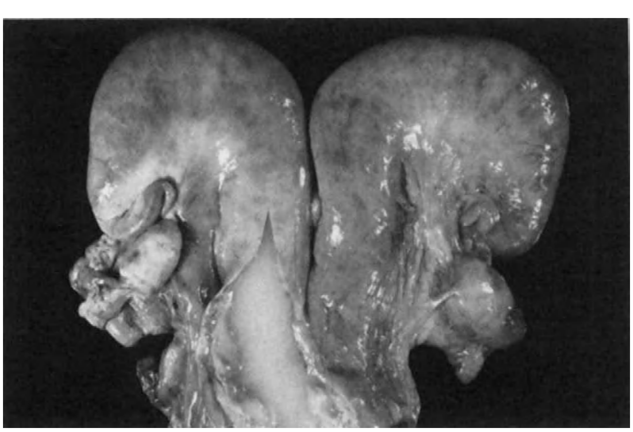

Fig. 11.4. Bovine uterus containing 250 ml of cloudy mucus associated with small follicular cysts. Hemorrhagic cyst in right ovary. Acc. No. 18122.

Ewe and Doe (Goat)

Hydrometra of undetermined etiology occurs in the ewe and doe. Smith (1980) reported that "Hydrometra is a significant cause of infertility and abdominal distention in the goat. The uterus is thin-walled and contains thin, clear fluid. Several liters of liquid may be present." The endometrium is thin, and the glands are slightly dilated. The cervical lumen and the cervical glands are filled with mucus.

During the examination of reproductive tracts from slaughtered nonpregnant ewes, Adams (1975) found 3 uteri with hydrometra in a series of 487 animals, and Emady *et al.* (1975) reported 3 cases in 1982 ewes.

Gilt

Einarsson and Gustafsson (1970) found 33 cases of hydrometra during the postmortem examination of the reproductive tracts of 1000 gilts. Thirty-one of the cases occurred in prepuberal gilts. The uterine horns were evenly distended with clear yellow mucoid fluid, and the uterine walls were very thin. The fluid is usually expelled during the first estrus.

Mare

I have examined the uteri from four 22- to 27-year-old mares with mucometra. Three-tenths of a liter to 4 liters of gray to brown mucoid fluid were present in the uterine lumen. Cystic hyperplasia of the endometrium and a mild to severe lymphocytic infiltration of the endometrium were present in all the uteri. The inflammatory infiltrate extended to the depth of the endometrium in one case. Two mares had large areas of atrophy of the endometrium in the ventral part of the uterine body. Although the etiology of mucometra in the mare has not been established, it is associated with cystic endometrial hyperplasia and ventral atrophy of the endometrium in some mares. The two mares in which focal endometrial atrophy was not observed had abundant cytoplasmic mucus in the endometrial epithelial cells.

Bitch and Queen

Mucometra in the dog and cat is usually associated with endometrial hyperplasia due primarily to progesterone stimulation. Estrogenic stimulation can also cause the accumulation of fluid in the canine uterus. These conditions are discussed under endometrial hyperplasia. Mucometra also occurs in association with segmental aplasia of the uterus and aplasia of the cervix.

Adenomyosis

Adenomyosis is a benign condition characterized by the ingrowth of endometrium into the myometrium. It occurs mostly in the bitch, queen, and cow. Unfortunately, adenomyosis is frequently and incorrectly referred to as internal endometriosis. Endometriosis is a condition in which endometrium, including epithelium and stroma, is present in various locations outside of the uterus. It is a common lesion in women and nonhuman primates (Ridley, 1968; McCann and Myers, 1970) and occurs only in those species of mammals that menstruate.

When preparing uterine tissue for fixation, it is essential to open the uterine horns before placing the tissue in fixative. When the unopened uterus of an animal that has died recently is placed in fixative, contraction of the uterine muscle forces endometrium into the myometrium, producing an artifact resembling adenomyosis.

Adenomyosis may occur as a focal or diffuse lesion. All the grossly visible focal lesions that I have seen in dogs have occurred in the uterine body, which was firm and enlarged to several times normal size. The displaced endometrial glands in the myometrium are cystic and are visible on gross examination of the incised specimen.

When adenomyosis of the uterus occurs concurrently with pyometra, the inflammation may extend along the glands into the myometrium and even to the uterine serosa. On gross examination, small subserosal abscesses are evident and they can rupture spontaneously, causing peritonitis.

Dow (1962) reported adenomyosis of the uterine body in the cat. The condition was found in association with the cystic hyperplasia–pyometra complex.

Endometrial Hyperplasia

Excessive estrogenic stimulation induces hyperplasia of the endometrium in the cow, ewe, and bitch. Follicular cysts, granulosa cell tumors, and sustentacular cell tumors in male pseudohermaphrodites provide an endogenous source of estrogen. Exogenous sources include synthetic estrogens used for therapeutic purposes and clover pastures containing estrogenic compounds.

Prolonged or excessive progesterone stimulation induces a histologically different type of endometrial hyperplasia in the bitch and the queen. The naturally occurring disease follows repeated estrous cycles that are not interrupted by pregnancy. Synthetic progestational compounds may also induce endometrial hyperplasia in the dog and cat.

Bitch

Four distinct types of endometrial hyperplasia occur in the bitch: cystic hyperplasia–pyometra complex due to excessive progesterone stimulation, hyperplasia associated with pseudopregnancy, estrogen-induced hyperplasia, and endometrial polyps.

Cystic Hyperplasia–Pyometra Complex. This is one of the most important hormonally induced diseases in the bitch. It has been suggested by several workers that the condition is due to hyperestrogenism. However, Teunissen (1952) demonstrated that progesterone plays a major role in the production of the disease. Dow (1959a) conducted an extensive investigation of the experimentally induced disease. Slight glandular proliferation was induced by estrogen administration, but the changes did not progress to a very advanced stage. Daily injections of 10 mg of progesterone for a period of 60 days induced cystic hyperplasia of the endometrium in young ovariectomized bitches. The lesions developed more rapidly in bitches that were subjected to a priming treatment with estrogen followed by progesterone. The degree of hyperplasia was greater when the ovariectomized bitches were subjected to artificial cycles produced by 10 daily injections of 5 mg of stilbestrol followed by 20 daily injections of 10 mg of progesterone. The lesions induced by four artificial cycles were similar to those observed in naturally occurring cases.

Dow (1957, 1959a) examined the uteri from 100 bitches with the cystic hyperplasia–pyometra complex and classified the uterine lesions into four groups.

Group I. Animals in this group had endometrial hyperplasia without endometritis. The 23 dogs ranged in age from 3 to 12 years. Dow (1957) reported that 15 of the bitches "had shown some evidence of sexual abnormality before admission. Irregular occurrence of oestrus had been present in five bitches over a period of 1 to 4 years. In four bitches, there had been abnormal duration of pro-oestrus and oestrus which was extended to 30 days or more or was abbreviated to as little as 5 days." In a subsequent report dealing with a survey of the genitalia of 400 bitches submitted for routine postmortem examination, Dow (1958) stated that the significance of the "oestral abnormalities is doubtful since similar aberrations from the accepted normal were found in 19 of 53 bitches in the same age range and breeding history." Pseudopregnancy had been diagnosed clinically in seven of the affected animals and only in one of the controls. A mucous vaginal discharge was noted during metestrus but not at any other stage of the estrous cycle. The uteri were larger and more rounded than normal.

Fidler *et al.* (1966) compared the estrous cycle characteristics of bitches with pyometra with those in a series of control animals. They found that "There were no significant differences in the occurrence of estrous cycle irregularities, abnormal estrus, and pregnancy in 68 bitches with pyometra as compared with 245 age-matched control bitches. Pseudopregnancies were observed less frequently in those with pyometra than in the controls."

Dow (1959a) stated that "In many cases examined, 30 to 50 days postoestrus, the superficial and crypt epithelium has assumed a very florid, highly secretory appearance. . . . . The cytoplasm is palely eosinophilic and finely vacuolated. In late metoestrus, the cytoplasm of the superficial epithelium becomes almost completely vacuolated and fatty in appearance." *Eschericha coli* was isolated from some of the metestrual uteri, but no evidence of endometritis was present.

Group II. Plasma cells were present in the hyperplastic endometrium. The age of the 17 animals in this group ranged from 4 to 11 years. Thirteen of the bitches had not been pregnant, and the other 4 had had single pregnancies 5 to 9 years previously. Twelve animals had shown irregularities in their estrous cycles. "All were discharging a variable amount of glairy; mucoid fluid which, in many cases, had persisted for several weeks" (Dow, 1959a).

The uteri were enlarged, but the horns rarely exceeded 3 cm in diameter. Clear mucoid fluid was present in the uterine lumen. *Escherichia coli* was isolated from 14 uteri and 3 were negative on culture. The endometrium was thick, roughened, and dull gray and contained irregular cysts and polypoid lesions. The histologic lesions consisted of a marked cystic glandular hyperplasia with a diffuse infiltration of plasma cells.

Group III. Neutrophils and plasma cells were present in the hyperplastic endometrium. The 49 bitches in this group were 4 to 13 years of age. Thirty-eight had not been pregnant, and the rest had whelped 5 to 11 years previously. Fourteen bitches had shown irregularities in the estrous cycles. The average interval between estrus and examination was 30 days, the range was 5 to 80 days, and 77% were presented in the first 40 days postestrus. Vulvar discharge was noted in 38 bitches on admission. All the animals, except one, had shown listlessness and anorexia. Increased thirst had been noted in 32 cases. Emesis occurred in 21 bitches and was most severe in those with gross uterine distention.

"The size of the uterus was inversely proportional to the degree of patency of the cervix. Uteri weighing up to 3 or 4 kg, and with horns measuring 50 cm long and up to 7 or 8 cm in diameter, were not uncommon in 15- to 20-kg bitches" (Dow, 1959a). The uterus usually had annular constrictions, but in some cases the uterine horns were uniform in diameter. The uterine fluid was red-brown, yellow, or green. "The endometrial surface had a roughened appearance with mingling of smooth, pus-filled cysts, focal hemorrhages, and areas of ulceration." Bacteria were not isolated from five uteri. "Of the remainder, all but four yielded *E. coli,* six yielded a coagulase-positive staphylococcus, and five contained a β-haemolytic streptococcus." Histologically, there was an acute suppurative endometritis superimposed on cystic endometrial hyperplasia. The inflammation extended into the myometrium in 40% of the uteri. One bitch died of acute peritonitis following rupture of the uterine wall.

Group IV. The animals in this group apparently had repeated attacks of the acute disease. The mean age of the 11 bitches in this group was 11.8 years with a range of 9 to 15 years. Only two of the nine animals in which breeding histories were available had been pregnant. The bitches were presented for clinical examination between 55 to 90 days following estrus. The cervix was open in some animals and closed in others. "In the open cases, only discharge and slight inappetence were observed. The closed cases were seriously ill with increased thirst, frequent vomition, and prostration" (Dow, 1959a). Skin lesions were present in both types. "The skin was dry and inelastic, with areas of alopecia on the flanks, over the abdomen and on the perineal region."

The uterine horns were seldom more than 3 cm in diameter when the cervix was open. Only a small amount of muco-pus was present in the uterine lumen in these cases, and the uterine walls were thick. The uterus was distended, and the uterine walls were very thin when the cervix was closed.

The endometrium in the open cases was atrophic with few glands. The endometrial stroma was fibrotic and infiltrated by lymphocytes and a few plasma cells. The myometrium was hypertrophic and fibrotic.

The endometrium and myometrium were atrophied in the closed cases. Endometrial glands were sparse, and the endometrial epithelium had frequently undergone squamous metaplasia. "Bacteriological examination revealed no growth in 2 cases, *E. coli* in 8, *Staphylococcus aureus* in 2, and a β-haemolytic streptococcus in 2" (Dow, 1959a). Dow (1957) stated that "There is, as yet, no experimental evidence to link the chronic lesions with those in the other groups, but it is possible that they develop after a number of acute attacks as the history suggests. A lesion similar in most respects to Type IV was produced by ligating the uterus and then subjecting the animal to several artificial cycles."

Extragenital Lesions of Cystic Hyperplasia–Pyometra Complex. Bloom (1944) described the changes in the blood and bone marrow of bitches with the cystic hyperplasia–pyometra complex. The blood is characterized by a pronounced leukocytosis, a "shift to the left" and toxic changes, and "disturbed maturation levels of neutrophilic cells." He stated that "the bone marrow shows: (a) a marked hyperplasia, particularly of neutrophilic forms, (b) increased number of megakaryocytes, and (c) widespread toxic changes and disturbed maturation differentials of neutrophilic cells. The changes in the bone marrow readily explain the blood picture that is found in pyometra."

Schalm (1973) stated that "retention of a purulent exudate in the uterus exerts a chemotactic effect on neutrophil leukocytes. The magnitude of the total leukocyte count in pyometra may be in part a reflection of the degree of closure of the cervix." He presented a table of the hemogram of 16 bitches with pyometra. In addition to leukocytosis, some bitches have a slight to moderate normocytic normochromic anemia.

Bloom (1946) described the extragenital lesions of cystic hyperplasia–pyometra complex in the bitch. He stated that "The most conspicuous microscopic lesion consisted of heterotopic collections of myeloid cells in the spleen, kidneys, liver and adrenals. . . . The cellular components of the ectopic myeloid deposits consisted of myeloblasts, myelocytes, non-segmented and segmented neutrophils and megakaryocytes. Occasional eosinophils occurred, and cells of the erythroid series were absent." Degenerative changes were noted in the epithelium of the renal tubules. Intertubular infiltrates consisted of lymphocytes, plasma cells, and a few histiocytes. "The foci of extramedullary myelopoiesis were usually distinct from the inflammatory cells, but not uncommonly both groups were intermingled so that separation was difficult" (Bloom, 1946). A mild to moderate fatty change was found in the liver of most animals. The most prominent liver lesion was the "myeloid metaplasia that varied from small, isolated, cellular aggregates to large diffuse masses, so that the microscopic appearances were frequently similar to those seen in this organ in human myeloid leukemia" (Bloom, 1946). Extramedullary myelopoiesis was conspicuous in the spleen. The adrenal glands appeared normal in some bitches, others had areas of necrosis and hemorrhage, and some had moderate to extensive areas of myeloid metaplasia. The septal capillaries and the large blood vessels in the lung were congested, and the capillaries "were often plugged with non-segmented and segmented neutrophils. Megakaryocytes, most of which had pyknotic nuclei, were present in the septal walls. The follicles in the lymph nodes were usually hyperplastic and often contained secondary nodules" (Bloom, 1946).

The pathogenesis of the renal lesions in the bitch with cystic hyperplasia–pyometra complex was investigated by Åsheim (1965). Dogs with pyometra have polydipsia and polyuria. A deficiency in the hypothalamic neurosecretory system is not likely the cause of reduced urine-concentrating ability, because antidiuretic hormone is excreted in normal amounts and the histologic appearance of the hypothalamus and pituitary is normal. The inability of affected bitches to concentrate urine appears to primarily involve the kidneys. Åsheim (1965) stated that "The reduction in renal concentrating ability in bitches with pyometra can be referred partly to a reduction of the sodium gradient in the medulla and partly to reduced permeability of the distal tubules for water. Renal dysfunction could be reproduced experimentally by giving large doses of *E. coli* toxin. There were no obvious morphologic changes corresponding to the dysfunction nor could a relation be demonstrated between the defect in concentrating ability and the glomerular damage." Bitches with pyometra have membranous glomerulonephritis or a mixed proliferative and membranous glomerulonephritis (Obel *et al.*, 1964).

Medroxyprogesterone Acetate-Induced Endometrial Hyperplasia. The adverse effects of treating bitches with medroxyprogesterone acetate to shorten or prevent estrus have been reported by Anderson *et al.* (1965) and Brodey and Fidler (1966). The uterus becomes distended with gray to tan mucoid material. More mucus accumulates before infection becomes established than in naturally occurring cases. The hyperplasia of the endometrium involves primarily the surface and cryptal epithelium, which is tall columnar and has finely vacuolated cytoplasm. The crypts are widely distended with mucus. The glands in the basal zone are moderately dilated and lined by low columnar cells without cytoplasmic vacuolation.

Pseudopregnancy (False Pregnancy, Phantom Pregnancy, Pseudocyesis). In regard to pseudopregnancy in the bitch, Whitney (1967) stated that "The clinical signs appear some two months after oestrus and vary in their integrity from a mild abdominal distention and mammary hyperplasia to an almost complete replication of parturition and lactation, these changes being behavioral as well as physical." A mucoid or occasionally bloody mucous vulvar discharge may occur. There is no breed nor age predisposition for development of the lesion. It occurs in some young animals after their first estrus as well as in aged bitches, some of which have had several pregnancies. Sokolowski (1973) stated that "surgical uterine trauma results in a localized pseudopregnant state of the endometrium."

Johnston (1980) reported that "Overt pseudopregnancy has been observed 3 to 4 days after surgery in several bitches ovariohysterectomized during diestrus, in the luteal phase." She pointed out that this is not surprising since lactation and nesting occur in the pregnant bitch following luteolysis and the sharp decline in progesterone.

Allen (1986) stated that "It is now clear that, although mammary development is probably stimulated by progesterone, the occurrence of pseudopregnancy is not directly related to this hormone and is unlikely to be associated with uterine lesions. The finding of elevated concentrations of circulating prolactin supports the theory that prolactin is the causal agent. This also explains why a variety of steroid hormones are also effective in treatment, presumably because they inhibit prolactin release by the pituitary gland."

The gross uterine lesions consist of one or more focal areas of endometrial enlargement (Fig. 11.5). Mucus, which may be blood-tinged, is present in the uterine lumen. The margins of the enlarged areas of the endometrium may be green (due to hemorrhage) and simulate the maternal placenta of the pregnant bitch.

The lesion consists of polypoid projections of the surface and cryptal epithelium into the uterine lumen (Fig. 11.6). The hyperplasia progresses to the extent that the uterine lumen is nearly occluded. Numerous, small, basal vacuoles are present in the cytoplasm of the surface and cryptal epithelial cells. The crypts are filled with mucus. Papillary projections of the cryptal epithelium extend into the mucus-filled spaces. The glands in the basal zone of the endometrium are evenly dilated and lined by cuboidal epithelium. Similar but less marked changes are present in the endometrium between the enlarged areas. Regression of the lesion starts with necrosis in the hyperplastic tissue adjacent to the uterine lumen and the necrotic tissue sloughs into the uterine lumen. The sloughed tissue may become compressed into long thin masses. Such specimens, when passed from the vagina, have been mistaken for parasites.

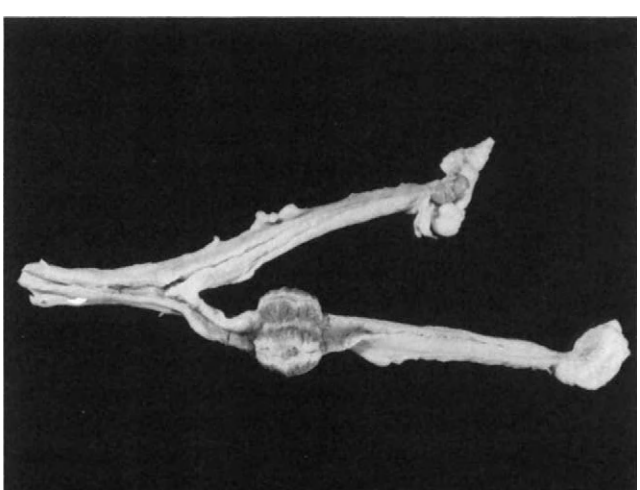

Fig. 11.5. Focal area of enlargement of endometrium in a pseudopregnant bitch. Acc. No. 17073.

Fig. 11.6. Proliferation of the cryptal epithelium and cystic endometrial glands in a pseudopregnant bitch. ×21. Acc. No. 18183.

Estrogen-Induced Cystic Endometrial Hyperplasia. Estrogen-induced hyperplasia of the endometrium occurs in some bitches with cystic follicular degeneration and in some with granulosa cell tumors. It can be induced by the administration of certain estrogenic compounds. Schwartz *et al.* (1969) found that the daily oral administration for 1 year of 100 μg/kg of a long-acting synthetic estrogen, quinestrol, caused marked endometrial hyperplasia and myometrial hypertrophy. Nelson *et al.* (1973) reported that the administration of 2 μg/kg/day of estradiol benzoate intramuscularly for 30 days to 10- to 12-week-old Beagle bitches produced moderate glandular and stromal proliferation.

Cystic hyperplasia of the endometrium occurs in male pseudohermaphrodite dogs with sustentacular cell tumors (Brown *et al.*, 1976). Some of these intersex dogs develop pyometra (Kelley *et al.*, 1976).

Estrogen-stimulated glands are widely dilated and form oval to spherical cysts. The surface and glandular epithelium consists of cuboidal to low columnar cells. With the exception of some of the intersex dogs with pyometra, there is usually no inflammatory reaction in the endometrium.

Endometrial Polyps. Endometrial polyps consist of focal areas of benign proliferation of endometrial glands and stroma. They may be solitary or multiple, broad or narrow based, and may occur in any portion of the endometrium of the dog and cat (Figs. 11.7 and 11.8). Although Andersen and Simpson (1973) classified the lesion as an adenoma, I consider endometrial polyps in domestic mammals to be a benign focal hyperplasia of endometrial glands and stroma.

Bloom (1954) stated that "The designation "polyp" refers to the gross and not to the histologic appearance of a pedunculated growth in the uterine cavity. The term is a poor one unless qualified by microscopic examination. . . .True endometrial polyps consist of endometrial tissue which may be normal or hyperplastic. Cyclic changes characteristic of the different phases of the estrous cycle may be observed in those with normal endometrium." He also stated that "Opinions vary as to whether endometrial polyps represent a focus of hyperplasia due to hyperestrinism or whether they represent benign adenomas, although the former supposition is more probable."

Gelberg and McEntee (1984) reported endometrial polyps from seventeen 4- to 12-year-old bitches. Most of the lesions were solitary, and they protruded into the vagina in four bitches. One dog with a 4.5 x 3.2 x 2.4-cm endometrial polyp protruding into the vagina (Fig. 11.9) had whelped 9 weeks prior to examination. Three bitches had torsion of the uterine horn containing a polyp. The uterine enlargements were detected on abdominal palpation in some cases.

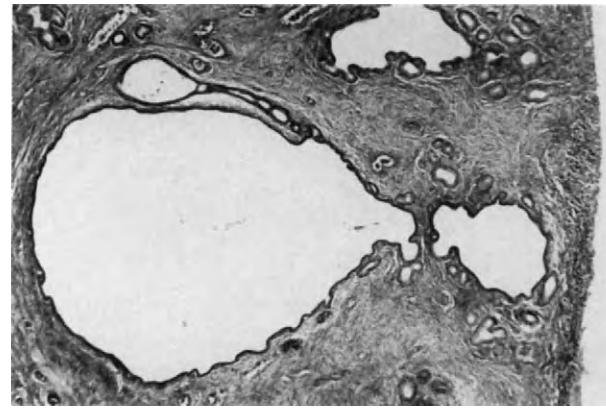

Fig. 11.8. Feline endometrial polyp. × 118. Acc. No. 673.

The polyps consist of cystic glands in a rather abundant endometrial stroma. The cysts may be lined by either cuboidal or columnar cells. When the cells are columnar, there is often papillary infolding of the epithelium lining the cysts. Small glandular formations extend from the cysts into the adjacent stroma. Focal areas of squamous metaplasia are present on the surface and in some of the glands in the large

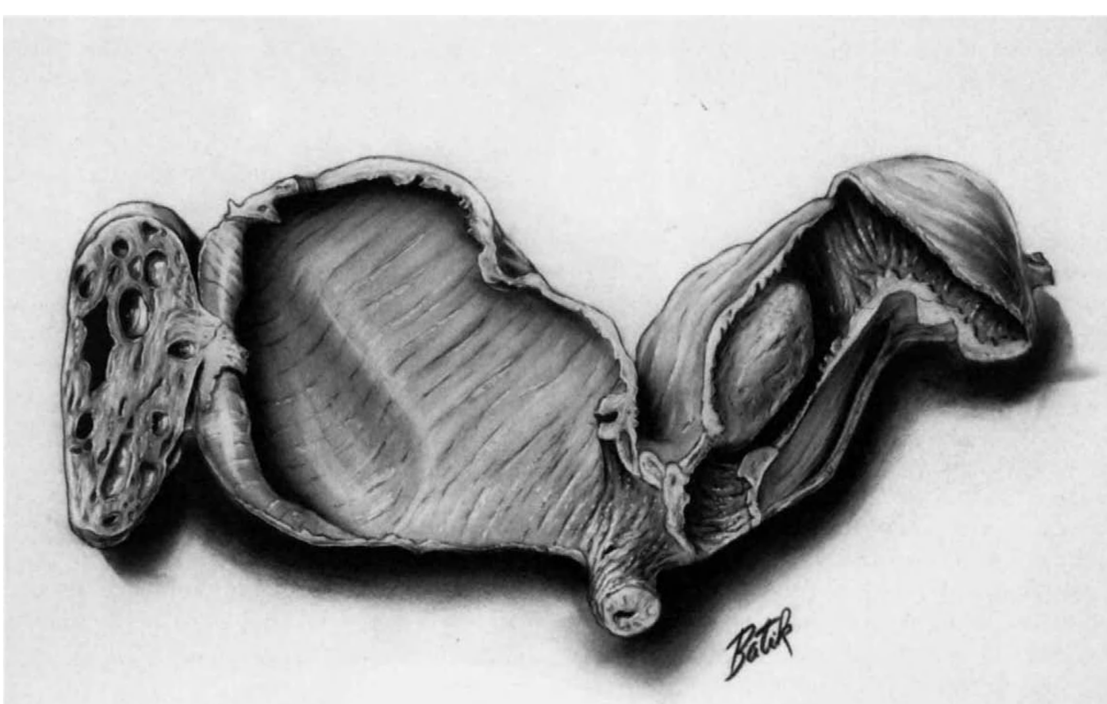

Fig. 11.7. Feline endometrial polyps. The polyp in the left uterine horn was incised to show the cystic glands. Acc. No. 673.

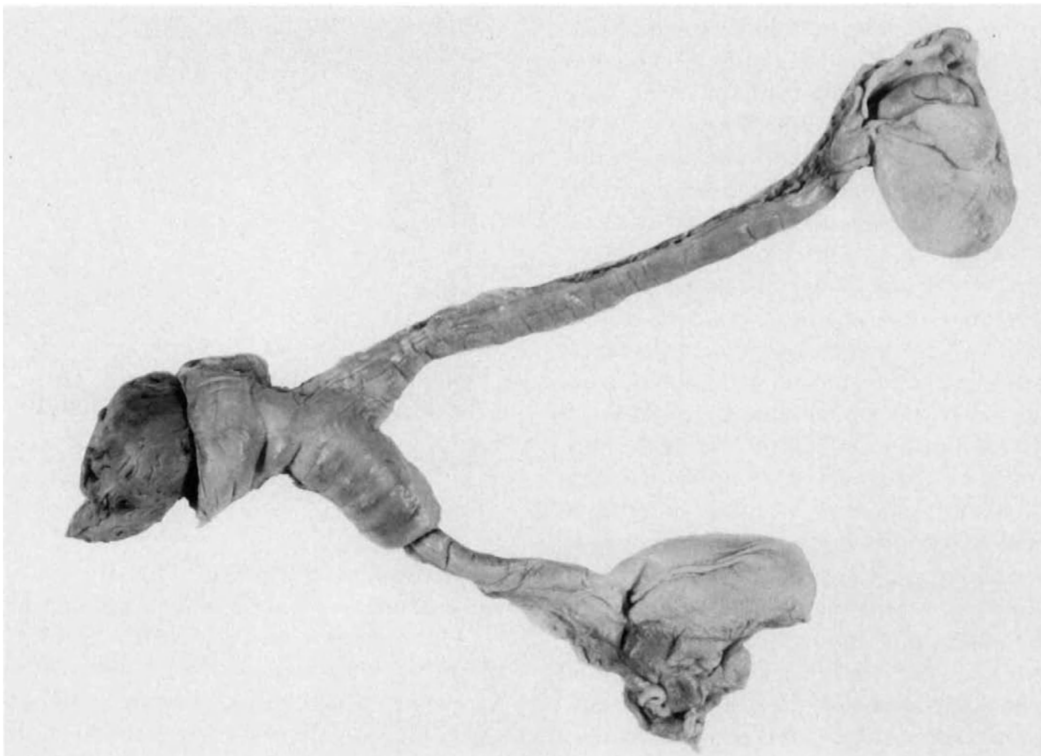

Fig. 11.9. Canine endometrial polyp protruding into vagina and causing inversion of a portion of the right uterine horn. Acc. No. 3877. (From Dobberstein *et al.*, 1985.)

polyps. The stroma consists of loosely arranged, spindle-shaped cells. Hemorrhage and/or inflammation may be present. Areas of ulceration and neutrophilic infiltration occur in polyps that protrude into the vagina.

Queen

Cystic Hyperplasia–Pyometra Complex. Dow (1962) reported 91 cases of the cystic hyperplasia–pyometra complex in the cat. He divided the cases into four groups on a morphologic basis.

Group I. Twenty cats, 3 to 14 years of age, had cystic endometrial hyperplasia without superimposed inflammatory lesions. The uterine lesions were found in five animals that had been submitted for routine postmortem examination because of other diseases and had not shown clinical evidence of genital disease. The uterus was surgically removed from four queens with a history of vulvar hemorrhage. Three of these had discharged blood for 10 to 14 days and were anemic with "erythrocyte counts of two to three million per cm and hemoglobin concentrations of less than 5 g per 100 ml. The blood smears in each case showed distinct normoblast and reticulocyte reactions" (Dow, 1962).

Dow (1962) reported that "The uteri in the majority of cases were only slightly larger than normal, and the endometrium was lined by a variable number of translucent cysts." The cysts were small and covered the endometrium in some uteri, "but in most, they were larger and occurred singly or in small groups at scattered points throughout the organ." Endometrial polyps were present in eight uteri. Torsion of the larger polyps had caused the vulvar discharge of blood in four animals.

The histologic lesions consisted of "either a diffuse hyperplasia of all glandular elements throughout the endometrium, or more commonly as a focal change affecting small groups at scattered points. Cystic dilatation of glands was prominent in some uteri and slight in others" (Dow, 1962).

The stage of ovarian activity varied greatly. The following were found in different queens: "recent or regressing corpora lutea, luteal remnants, normal follicular development and follicular cysts. The secretory activity of the hyperplastic endometrium correlated with the functional status of the ovaries" (Dow, 1962).

Group II. Thirty-nine clinically ill cats had cystic endometrial hyperplasia with superimposed acute endometritis. The age range of the affected queens was

3 to 11 years and 25 were nulliparous. The interval between parturition and examination in the parous cats ranged from 1 to 8 years. The duration of illness ranged from 3 days to 4 weeks. The clinical signs included dullness, depression, anorexia, vomiting, resentment to handling, and a green, brown, or red vulvar discharge. Vaginal smears revealed the presence of large numbers of neutrophils. The leukocyte counts of blood "ranged from 23,000 to 74,000 cells per mm^3 and tended to be highest in those cases with gross uterine distention and in those with myometrial involvement. Leukocytosis was due to an absolute increase in the numbers of neutrophils of which up to 30 percent were immature forms, principally, nonlobulated cells; myelocytes were observed in 15 percent of the samples examined" (Dow, 1962). The hemoglobin levels and erythrocyte counts were normal in most of the cats.

The volume of uterine exudate ranged from a few milliliters up to 1.5 liters. "The fluid was commonly a thick viscid yellow-green mucopus in the smaller uteri, but in the larger ones it tended to be more watery and of a brown or reddish color" (Dow, 1962). *Escherichia coli* was isolated from most of the uteri. Corpora lutea were present in the ovaries of 33 cats, normal follicles in 2 cats, and cystic follicles in 4 cats.

"The uterine lesions of these animals were characterized by acute inflammatory changes of varying severity superimposed on endometrial cystic hyperplasia" (Dow, 1962). The inflammation extended into the myometrium in more than 50% of the uteri. Large endometrial polyps were present in two uteri.

Group III. Ten queens had subacute endometritis superimposed on cystic endometrial hyperplasia. The affected cats ranged in age from 4 to 11 years. Seven were nulliparous. All the affected cats had histories of illness extending over at least 2 months. The signs of illness included depression, anorexia, abdominal distention, vulvar discharge, and loss of weight. The total leukocyte counts ranged from 21,000 to 32,000 per mm^3 with an absolute increase in the number of neutrophils, most of which were mature.

The uteri were moderately enlarged and contained 10 to 15 ml of green-gray viscid muco-pus in most cases. The cervix was patent in these cases. The cervix was closed in two animals, and the uterus in these queens contained about 200 ml of exudate. The uterine fluid was cultured from nine cats and *E. coli* was isolated from all specimens. Corpora lutea were present in the ovaries of nine cats and normal follicles in the tenth animal.

The histologic lesions consisted of cystic endometrial hyperplasia accompanied by a subacute endometritis with a diffuse infiltration of plasma cells and round cells in the superficial half of the endometrium. The surface epithelium was ulcerated, and multifocal abscesses were present in the endometrium. Granulation tissue was present beneath the ulcers and surrounding the abscesses. Dow (1962) stated that "there was considerable hypertrophy of both layers of the myometrium accompanied by increased intramuscular connective tissue." Two cats had adenomyosis of the uterine body.

Group IV. Twenty-two 5- to 14-year-old queens had chronic endometritis superimposed on cystic endometrial hyperplasia. Fourteen were nulliparous. The clinical signs included intermittent vulvar discharge for periods of 3 to 10 months and "occasional exacerbations of the illness characterized by abdominal enlargement and inappetence followed by profuse discharge and apparent improvement. Eight cats were seriously ill and some were in a state of collapse when presented" (Dow, 1962). The total white cell counts ranged from 24,000 to 61,000 per mm^3 with an absolute increase in the number of neutrophils. The erythrocyte counts and hemoglobin levels were within normal limits in most of the animals.

The uterus was moderately enlarged and contained only a few milliliters of exudate when the cervix was patent and the queen had a vaginal discharge. The endometrium in these animals was thin, atrophic, and fibrotic and contained only a few glands, some of which were polypoid in structure. A few plasma cells were present. The myometrium was atrophic and fibrotic.

The cervix was constricted in seriously ill cats, and the uterus contained a large amount of watery, brown-red fluid. All layers of the uterine wall were atrophic in cats with a closed cervix, and the endometrium was very thin and diffusely infiltrated by round cells. Squamous metaplasia of the surface epithelium was present in some uteri. *Escherichia coli* was isolated from the uterine exudate in most cases and a β-hemolytic streptococcus from about 30%. Corpora lutea were present in the ovaries of 18 cats, normal follicles in 2 cats, and cystic follicles in 2 cats.

Seventy-seven percent of the affected cats whose breeding history was available were nulliparous and only 8% were multiparous. At least 3 years had elapsed since the last parturition in most cats. Dow stated that "the results of this study indicate that the cystic hyperplasia–pyometra complex in the cat is basically similar to the disease observed in the bitch."

Medroxyprogesterone Actetate-Induced Endometrial Hyperplasia. Thornton and Kear (1967) reported that a young cat developed cystic endometrial hyperplasia following treatment with 1 ml of medroxyprogesterone acetate at 5 1/2 months of age to terminate pregnancy. At 9 months of age, the cat had a profuse, green-white vaginal discharge and the abdomen was slightly distended. The cat was ovariohysterectomized and hemolytic coliform organisms were isolated from the uterus. The uterine lesion consisted of "severe cystic hyperplasia of the endometrium with little evidence of acute inflammation" (Thornton and Kear, 1967). The lesions were considered to be similar to those in Dow's Group I cases.

Pseudopregnancy. Foster and Hisaw (1935) studied experimentally induced ovulation and the resulting pseudopregnancy in cats. "Optimal conditions for ovulation were apparently met by inducing follicular growth with purified F.S.H. and then injecting F.S.H. which contained approximately 0.1 percent L.H. intravenously" (Foster and Hisaw, 1935). The experimentally induced pseudopregnancy lasted 40 to 44 days. The histologic lesions consisted of papillary infolding of the surface epithelium, "a dilatation and coiling of uterine glands, a decrease in the height of uterine epithelium and a swelling of glandular epithelium especially in the basal region."

Endometrial Polyps. The gross and microscopic appearance of endometrial polyps is similar in the dog and cat (Gelberg and McEntee, 1984). However, the polyps are more frequently multiple in the queen than in the bitch. In contrast to the bitch, I have not seen endometrial polyps protrude into the vagina in the queen.

Cow

Cystic endometrial hyperplasia in the cow is due to chronic estrogen stimulation and is seen mainly in cows with long-standing follicular cysts and in some cows with granulosa cell tumors. Cows with cystic ovarian follicles and mucometra may have a variety of uterine lesions, including dilated endometrial glands, hyperplastic glands with varied degrees of cyst formation, or extreme atrophy of the endometrium superimposed on a preexisting hyperplasia. The hyperplastic glands are lined by columnar cells with papillary infolding. Some of the glands become distended with proteinaceous and/or mucoid material. The height of the epithelium is reduced in the large cysts. All the cows with mucometra associated with follicular cysts have myometrial atrophy. The atrophy is extreme when associated with endometrial atrophy. In these animals, the endometrial epithelial cells and the myometrial cells have very little cytoplasm.

Ewe

Bennetts *et al.* (1946) reported a severe progressive infertility problem, commonly known as clover disease, in ewes grazing on subterranean clover pastures in Australia. Plant estrogens (phytoestrogens including genestein, biochanin-A, daidzein, formononetin, courmarin, and coumestrol (Guggolz *et al.*, 1961) are present in various species of clover. Formononetin is considered the most important (Patroni *et al.*, 1982). Affected ewes have infertility, dystocia, and uterine prolapse, which generally occurs some months after parturition and which may affect even unbred animals. Udder development and milk secretion occur in young virgin females and unbred ewes. The infertile ewes manifest estrus but fail to conceive.

Macroscopic examination of the uterus reveals the presence of from a few to large numbers of cysts widely distributed throughout the uterus. The cysts are colorless, raised, and transparent and vary in diameter from about 0.1 to 1.5 cm. Schinckel (1948) reported that the infertility problem persists even when ewes are moved to pastures that are free of plant estrogens.

Adams (1976) conducted a morphologic and histochemical study of the uteri of 34 ewes with permanent clover infertility and compared the findings with 15 control ewes. Cysts of 2 to 8 mm in diameter were scattered throughout the endometrium of the phytoestrogen-exposed ewes and in two control ewes. The controls were aged ewes, and the cysts in these ewes may have developed during postpartum uterine involution. No changes were found in the ovaries. Groups of dilated and hyperplastic endometrial glands were present in the phytoestrogen-exposed ewes but not in the controls. Seven exposed ewes had adenomyosis, seven had acute endometritis, and five had chronic endometritis. Cattle may also be affected, but the condition has not been studied as thoroughly as it has in sheep (Thain, 1965b; Donaldson, 1983).

Underwood *et al.* (1953) induced cystic hyperplasia of the endometrium in sheep by injecting diethylstilbestrol intramuscularly, on alternate days, for a period of 6 months. The dose levels ranged from 1 to 16 mg per day. They reported that "the reproductive disturbances and the cystic endometrium obtained with the prolonged stilbestrol injections and their persistence for several years after cessation of treatments are identical with those previously recorded for ewes grazed on subterranean clover-dominant pasture."

Sow and Mare

Cystic endometrial hyperplasia occurs in the sow and mare, but the etiology and significance of the lesion have not been established.

Gimbo (1955) reported the presence of an endometrial polyp in a sow.

Hyperplasia of the Uterine Serosa

The long-term administration of synthetic estrogens to the bitch induces papillary proliferation of the uterine and mesometrial serosa (Mawdesley-Thomas and Sortwell, 1968). The lesion resembles the proliferation of the serosal surface of the ovary induced by chronic stilbestrol administration. O'Shea and Jabara (1971) reported that "there is no evidence that serous membranes of non-genital organs are capable of a primary proliferative response to stilbestrol."

Neoplasia

Uterine neoplasms in domestic mammals have been reviewed by Cotchin (1956, 1964) and Cotchin and Marchant (1977). The majority of epithelial tumors of the uterus are malignant, and most of the mesenchymal tumors are benign. The World Health Organization (WHO) classification of uterine neoplasms devised by McEntee and Nielsen (1976) is given in the following sections.

Epithelial Tumors

Adenoma. If fibroadenomatous polyps of the endometrium are considered to be hyperplastic rather than neoplastic lesions, endometrial adenomas are extremely rare in domestic mammals.

Adenocarcinoma. There are very few reports of uterine adenocarcinomas in domestic mammals, except in the cow.

Cow. Monlux *et al.* (1956) reviewed the literature on uterine adenocarcinomas in the cow and reported 26 cases. The cows ranged in age from 2 to 14 years. Eleven Herefords, 1 Brown Swiss, and 14 cows of unknown breeds were affected. Twenty-two of the 26 uterine carcinomas had metastasized to the lungs, 21 to lymph nodes, and 14 to the peritoneum. They compared 62 cases of metastatic adenocarcinomas found in the lungs, lymph nodes, and peritoneum of cows in which the uteri were not examined with the 26 cases of confirmed uterine carcinomas and stated the "metastatic lung, peritoneal and lymph node lesions in these 62 cases were indistinguishable from the metastatic lesions of known uterine carcinomas." It was obvious from their investigation that uterine carcinomas in the cow have been frequently overlooked during routine meat inspection. They stated that "the recovery and identification of uteri containing small primary tumors is difficult in most abattoirs due to the accepted practice of discarding these organs after a cursory inspection for gross abnormalities." In some abattoirs, the uterus does not even receive a cursory examination.

Brandly and Migaki (1963) reported 116 cases of endometrial carcinoma in the cow, and Migaki *et al.* (1970) reported an additional 192 cases from federally inspected abattoirs in the United States. The progressive increase in the number of reported cases is probably a result of the increased awareness of the lesion by federal meat inspectors. Migaki *et al.* stated that the endometrial carcinoma "is a commonly observed carcinoma in older cows." They also reported that "Reliable statistics on the incidence of bovine uterine adenocarcinoma are not available." They confirmed the statement by Monlux *et al.* that "Subsequent investigations may bear out our contention that the adenocarcinomas of the uterus rank only behind squamous cell carcinoma of the eye and its appendages and the lymphoid tumors in causing economic loss to the cattle industry."

Dukes *et al.* (1982) diagnosed 53 uterine carcinomas and 738 lymphosarcomas collected during the slaughter of 17 million cattle in Canada. Reports from Europe indicate that the uterine carcinoma is rare in cattle (Cotchin, 1964). Lagerlöf and Boyd (1953) found only one uterine carcinoma during the examination of the reproductive tracts from 6286 cows.

Although many cases of bovine endometrial carcinomas have been reported from the federal meat inspection service in the United States, it is not a common lesion in cattle. I examined nine endometrial adenocarcinomas from New York State cattle during a 33-year period. Only four of the cows had been examined by clinicians at the New York State Veterinary College. The other five specimens were collected from abattoirs, and clinical histories were not available. The breeds included four Holsteins, two Herefords, one Ayrshire, and two unknown. The Holstein breed is predominant in New York State.

Since the condition is rare and very few cases are diagnosed clinically, little information is available concerning the clinical history of affected animals. Loss of weight, emaciation, dyspnea, and infertility have been recorded. The lesions have been misdiagnosed as tuberculosis on clinical examination.

The gross uterine lesions are characteristic and should enable an informed veterinarian to make an accurate clinical diagnosis. One or more moderately enlarged, firm, constricted lesions are present in the uterus (Fig. 11.10). The surface of the endometrium usually appears to be normal. The cut surface of the neoplasm is hard, white to yellow, and may have calcified areas. Metastases occur predominantly in the internal iliac lymph nodes and in the lungs (Fig. 11.11). Metastatic lesions may occur in sublumbar, mediastinal, and bronchial nodes, on the surface of the liver,

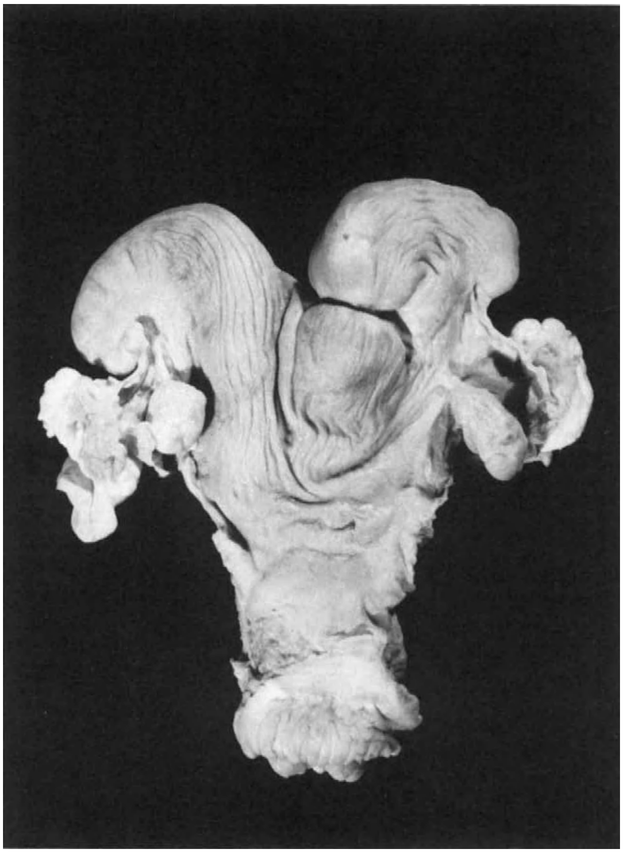

Fig. 11.10. Bovine endometrial carcinoma causing indentation of myometrium. Acc. No. 14314.

spleen, gastrointestinal tract, and peritoneum, and in the ovaries, kidneys, adrenals, and myocardium (Migaki *et al.*, 1970). The gross appearance of the metastatic lesions is similar to that of the primary carcinoma.

The lesion appears to start deep in the endometrium and tends to extend into the myometrium (Fig. 11.12) rather than growing into the uterine lumen. "The uterine glands located deep in the lamina propria were hyperplastic, and transformation of the epithelial cells of the glandular structures into neoplastic cells could be seen" (Migaki *et al.*, 1970). The neoplastic epithelial cells are large and pleomorphic and have abundant eosinophilic cytoplasm. The nuclei are large and vesicular, and mitotic figures are frequent. Solid cords and glandular formations are present in a very abundant fibrous tissue stroma, and some areas of the neoplasm are composed predominantly of stroma. Tumor thrombi are present in veins and lymphatics.

Mare. Gunson *et al.* (1980) reported an adenocarcinoma of the uterus of a 14-year-old, emaciated mare with chronic obstructive pulmonary disease (heaves). The mare had anorexia, a mucoid nasal discharge, and rales. Radiographs revealed intrapulmonary

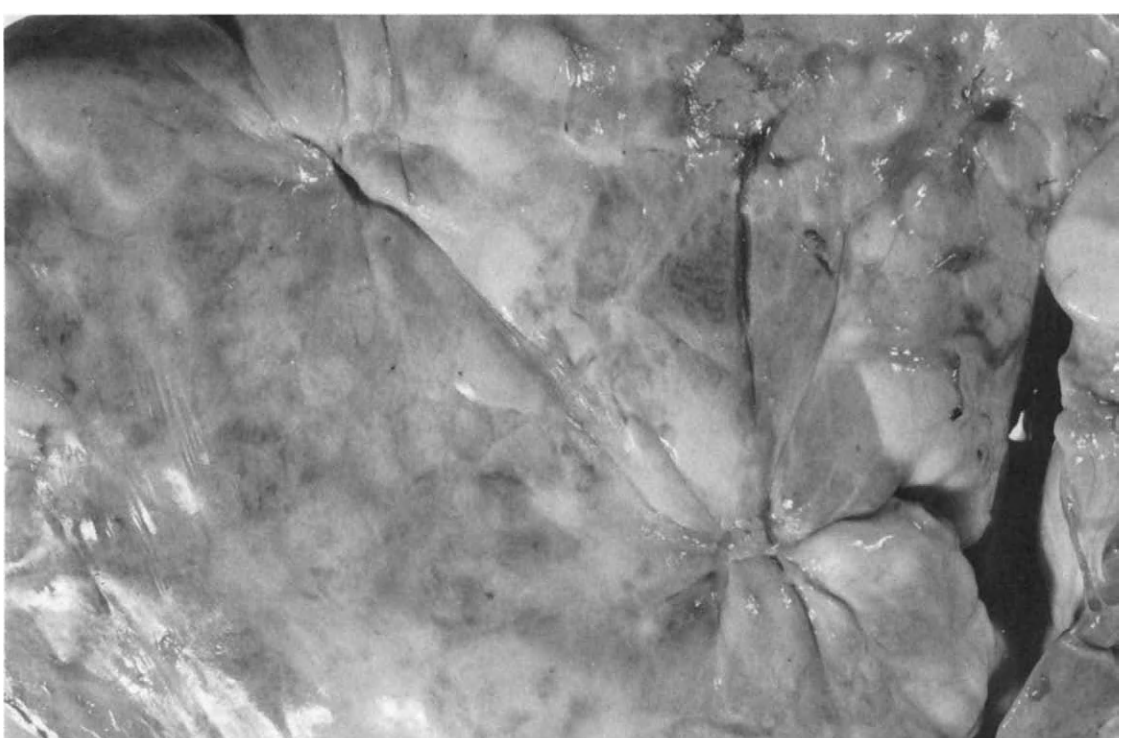

Fig. 11.11. Multiple indented areas of pulmonary metastases of a bovine endometrial carcinoma. Acc. No. 14314.

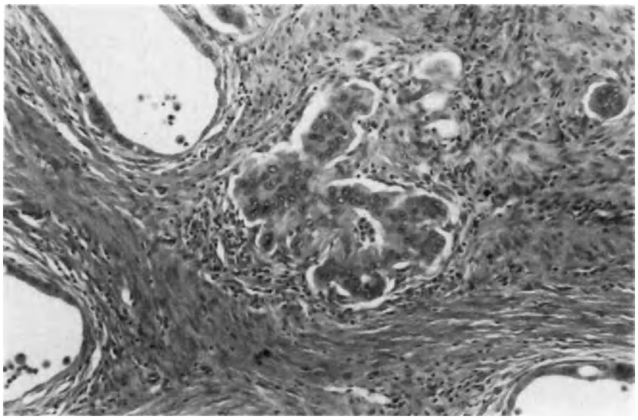

Fig. 11.12. Bovine endometrial carcinoma in myometrium. ×89. Acc. No. 14314.

masses. One firm mass was palpated in the uterus and several in the abdominal cavity.

At necropsy, "The uterus was of normal size and shape. There was a hard thickening over a 3-cm area at the bifurcation, where the wall was 2 cm thick. The left horn had two smaller but similar thickenings" (Gunson *et al.*, 1980). The endometrium contained several 5-mm cysts. The internal iliac lymph nodes were of normal size but hard, "orange-brown, and mucoid on cross section." Many firm, pale masses 1 to 10 cm in diameter were present in the lungs. A 30-cm neoplasm was present in the cranial part of the right diaphragmatic lobe.

The uterine neoplasm consisted of anaplastic glandular tissue (Fig. 11.13) extending from the endometrium into the myometrium. Many of the neoplastic glands were filled with mucus. Lymphocytes and plasma cells were scattered in the fibrous tissue stroma. The stromal fibrous tissue was not as abundant as in uterine adenocarcinomas in the cow. The lymph node and lung lesions were similar, but the metastatic lesions in the lungs were producing more mucus.

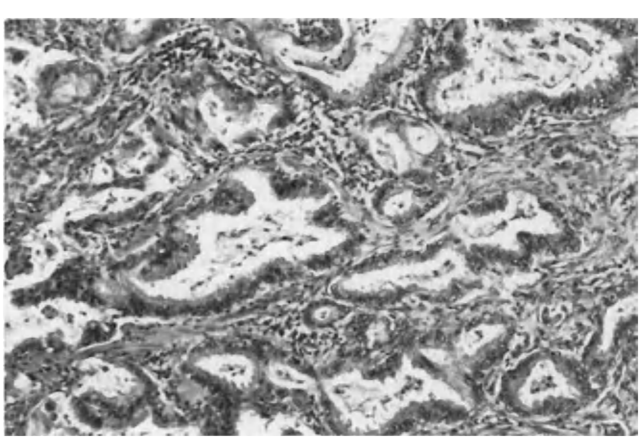

Fig. 11.13. Equine endometrial carcinoma. ×89. Acc. No. 19142. (Tissue provided by D. E. Gunson.)

Sow. I am aware of only two uterine carcinomas that have been reported in domestic swine (Loeb, 1900; Werdin and Wold, 1976). The neoplasm reported by the latter authors consisted of large, highly cellular masses of neoplastic epithelial cells surrounded by dense fibrous tissue. Acinar formation was a distinct feature of the neoplasm, and mitotic figures were numerous.

Doe (Goat). Brandly and Migaki (1963) recorded a uterine adenocarcinoma in a goat but did not present information concerning the gross and microscopic features. Riedel (1964) reported an endometrial adenocarcinoma in a 12-year-old goat. Metastases were present in the iliac, mediastinal, and mammary lymph nodes and in the liver, spleen, uterine tube, ovary, and skeletal muscle.

Ewe. Terlecki and Watson (1967) reported a uterine adenocarcinoma in a 5-year-old ewe that was "listless, off its food, and from distention of the abdomen was thought to be pregnant." About 1 1/2 liters of fluid were present in the peritoneal cavity. "The colonic mesentery was thickened and covered with nodular gelatinous growths. The cervix was thickened and its canal closed. The body and right horn of the uterus showed an irregular thickening of its wall" (Terlecki and Watson, 1967). Mucoid masses covered the endometrium. The broad ligament, wall of the urinary bladder, and terminal portion of the rectum were thickened.

Histologically, the neoplasm consisted of "solid groups of variable defined acini of neoplastic epithelial cells scattered throughout the tissues. The cells were highly pleomorphic and varied from tall columnar to small, shrunken dark forms" (Terlecki and Watson, 1967). Many of the cells contained mucin and mitotic figures were common. Fibrous stroma predominated in the metastatic lesions in the ovaries, bladder, and perirectal tissue.

Bitch. Cotchin (1964) reviewed the literature on uterine cancer in domestic mammals and stated that "I have found no good published photomicrographs of canine uterine carcinoma. There are a few reported cases, some of doubtful significance." He examined more than 6000 canine neoplasms without finding a single uterine carcinoma and stated that Head did not find any uterine carcinomas in a series of 8093 canine tumors. Brodey and Roszel (1967) did not find any uterine carcinomas in a series of 96 neoplasms of the uterus, vagina, and cervix in 90 bitches "derived from 3,073 tumor-bearing dogs seen out of a total population of 75,000 dogs."

Andersen (1963) reported a carcinoma of the uterus in a 10-year-old Beagle bitch that was on an experimental life-span evaluation of the effects of irradiation. She was given four whole-body x-ray exposures of 75 rads each at 7-day intervals at the age of 11 months. Subsequently, the bitch was bred and whelped two litters. The bitch had three estrous periods following the last parturition. Then she had either false estrus or was anestrus for 1300 days before death. He concluded that "the finding of a malignancy under these conditions could reflect a possible long-term effect of ionizing radiation."

A 1 x 4 x 4-cm tumor was present in the right uterine horn of this bitch. On cut section, it appeared as "a pulpy, cavernous mass." The neoplasm had metastasized to the lungs, bronchial lymph nodes, pericardium, liver, spleen, gastrointestinal tract, kidneys, and pancreas. A description of the histologic features of the neoplasm was not presented.

Koch and Kaiser (1976) reported an adenocarcinoma that occurred in the uterus of a 12-year-old bitch. Death followed massive metastases "in numerous organs, including the brain, heart and lungs."

Payne-Johnson *et al.* (1986) diagnosed a proliferative lesion that was found in the uterine body of a 3-year-old bitch as an endometrial carcinoma. The bitch had been treated with ethinyloestradiol and methyltestosterone for pseudopregnancy. The signs of pseudopregnancy regressed but were followed by polyuria and persistent licking of the vulva. The bitch was treated a second time with ethinyloestradiol and methyltestosterone. The vulvar discharge continued, thus the dog was treated with megoestrol acetate and urinary acidifiers. No improvement was noted after 18 days of this treatment, thus the bitch was ovariohysterectomized. The uterus "contained a large polypoid intraluminal mass with the histological features of endometrial carcinoma, the bitch has remained well for 31 months after surgery. The possibility is considered that the lesion is drug-related but no firm conclusion can be drawn about the precise nature and pathogenesis of this unusual lesion" (Payne-Johnson *et al.*, 1986). I believe that the uterine nodule was a hyperplastic lesion induced by the therapy for pseudopregnancy and the subsequent vaginal discharge.

The canine "uterine adenocarcinoma" reported by Joshi *et al.* (1967) may have been an endometrial polyp. The left uterine horn was "overdistended and twisted" and contained "an ulcerated, roundish and sessile cystic mass. The growth was composed of acinar cavities of irregular size and shape lined by a single layer of cells." The description of the gross and microscopic lesions fits that of an endometrial polyp. Furthermore, endometrial carcinomas in domestic mammals usually grow into the myometrium rather than into the uterine lumen. The "glandular elements—invading the myometrium" were not described in detail nor illustrated. The invasion of the myometrium by the endometrium may have been adenomyosis.

I have seen only two carcinomas in the canine uterus. Both were metastatic, solid carcinomas of mammary gland origin. One metastatic lesion was found in the myometrium only on histologic examination but was grossly evident in the right ovary. The other metastatic tumor presented as a 1 x 1-cm, soft, cream-colored mass in the endometrium. Numerous tumor thrombi were present in thin-walled vessels in the myometrium.

Schlotthauer (1939) and Riser (1940) reported single cases of canine uterine lesions that they considered to be chorioepitheliomas. The one described and illustrated by Schlotthauer is a case of pseudopregnancy, and that by Riser appears to be adenomyosis with areas of perforation of the uterine serosa. I am not aware of an authentic report of chorioepithelioma in domestic mammals.

Queen. Meier (1956) reported two cases of uterine carcinoma in the queen. An 11-year-old cat developed lethargy, anorexia, and constipation and was ovariohysterectomized. "Examination disclosed pallor, slight fever, and a rectal displacement due to a 'mass under the sacrum' " (Meier, 1956). The temperature dropped after antibiotic treatment but the fever returned and the cat was anemic a few days later. "The leukocyte count was 19,050 per mm^3 and the hemoglobin 5 mg per 100 ml of blood." The cat died and was necropsied.

"Multiple cystic masses were found in the peritoneal cavity involving the gastrosplenic omentum, mesocolon, ventral ligament of the bladder, the ligated end of the left uterine horn and a retroperitoneal mass in the left abdominal wall 3 cm posterior to the diaphragmatic insertion" (Meier, 1956). Cystic masses were found in the sublumbar region. The uterine horns had been cut about 2 cm cranial to the uterine body and the remnant of the left horn terminated in a cystic mass.

"The microscopic picture was that of an adenocarcinoma of the endometrial glands with spread by contact to the peritoneal surface and by lymphatics to the iliac lymph nodes" (Meier, 1956). Some of the cysts were filled with proteinaceous material and others contained neutrophils. The neoplastic cells in some of the glands were packed densely, and mitotic figures were numerous. The primary uterine tumor and the metastatic lesions were similar.

Meier's second case occurred in a 5-year-old cat with a history "of intermittent purulent vaginal discharge starting just after the last known heat period one year before" (Meier, 1956). The cat vomited occasionally and was thin. "A hard, lobular mass about 5 cm in diameter was palpable in the region of the bladder." Pyometra was diagnosed. The cat was ovariohysterectomized and apparently recovered but returned 1 month later because of vomiting and collapsing spells. Hard masses were palpated in the region of the sublumbar lymph nodes, and the cat was killed. "The right uterine horn was greatly enlarged and filled with a greenish, caseous, odorless material, which was especially dense in thick pouchings of the uterine wall."

The microscopic lesions consisted of a squamous cell carcinoma of the uterine wall associated with subacute metritis. Metastatic carcinomas were present in the pelvic, sublumbar, sternal, and bronchial lymph nodes and in the lungs, parietal pleura, heart, and liver. It was not determined whether the carcinoma originated in the cervix or uterus.

Preiser (1964) and O'Rourke and Geib (1970) reported single cases of uterine carcinomas in 11- and 12-year-old queens. The cat reported by Preiser "developed coprostasis and only a small amount of black, watery feces could infrequently be eliminated" during the 5 weeks prior to clinical examination. The presence of an abdominal tumor was suspected, and the cat was killed.

A 3 1/2-cm, white, "firm but friable, gelatinous, partially cystic, encapsulated growth" was present in the left uterine horn (Preiser, 1964). Tumor nodules were implanted on the mesometrium, peritoneum, and mesentery. Multiple "smaller than pea-sized, white pearl-like nodules" were present in the lungs, diaphragm, and liver. A single nodule was present in the right kidney.

Histologic examination of the uterine mass revealed areas of transition from hyperplasia to neoplasia of the endometrial epithelium. Preiser stated that the hyperplastic epithelial cells "undergo metaplasia and subsequent anaplasia appearing as very large, cuboidal, sometimes multinucleated, eosinophilic cells with large, hyperchromatic, often kidney-shaped nuclei; these cells have invaded down toward the myometrium." Mitotic figures were abundant, and multinucleated tumor cells were present. The anaplastic cells were found singly and "in distorted cords within a connective tissue matrix." The metastatic lesions were similar to those in the primary uterine neoplasm.

O'Rourke and Geib (1970) described an endometrial adenocarcinoma in a cat that was presented "with a history of dystocia two months previous in which one kitten was delivered dead and a second dead kitten was extracted from the vagina 24 hours later; recovery was uncomplicated." A black-green vulvar discharge occurred 1 month later, and the cat became uncoordinated and had partial blindness. Ocular examination revealed retinal detachment and hemorrhage in both eyes. The cat was killed.

The uterine horns were about 1 cm in diameter and appeared thickened and nodular. A transverse section of uterine horn revealed "a pearly-white tissue" that almost filled the lumen. Numerous translucent foci 1 to 2 mm in diameter were found in the brain. A large area of retinal detachment and hemorrhage was present in the right eye, and retinal hemorrhage and tears were present in the left eye.

Histologically, the uterine mass was found to be an endometrial adenocarcinoma "composed largely of densely packed epithelial cells with large vesicular nuclei, a distinct nucleolus, and indistinct cell boundaries. More typical acinar arrangement and cystic spaces were also formed" (O'Rourke and Geib, 1970). The neoplasm extended into the uterine lumen and into the myometrium. Metastatic adenocarcinomas were found in the ovary, adrenal, brain, lung, and eyes.

Mesenchymal Tumors

Fibroma. Pure uterine fibromas of the uterus are comparatively rare in domestic mammals. They are hard, white, spherical neoplasms of the uterine wall. They consist of dense masses of collagenous fibrous tissue.

Mahony (1890) reported the gross but not the microscopic lesions of multiple uterine tumors in a 2-year-old filly. A large "fleshy body" protruded from the vulva. Examination of the vagina revealed the presence of several tumors protruding from the cervix. A large growth was present within the uterus. The author stated that he had seen close to 50 similar cases in fillies sired by "a common bred stallion." Many of the tumors were necrotic. The occurrence of the lesions in fillies and their spontaneous regression suggest that the growths were probably due to a virus.

I have seen only one pure fibroma of the bovine uterus that occurred in the caudal portion of the left uterine horn of a 14-year-old Holstein-Friesian cow. A firm uterine mass was detected at the time of the parturition. The cow had poor fertility during the last 6 years of life. The last four calving intervals were 15, 16, 14, and 17 months, respectively. The number of services per pregnancy resulting in the birth of a calf were four, seven, four, and seven, respectively. Numerous intrauterine treatments with various antibiotics and Lugol's solution had been administered between pregnancies.

A spherical, encapsulated, hard, white mass measuring 14 cm in diameter and weighing 1202 g was surgically removed from the distal portion of the right uterine horn. The neoplasm consisted of dense collagenous fibrous tissue. No smooth muscle fibers were detected with Van Gieson's collagen fiber stain.

Fibrosarcoma. Fibrosarcomas of the uterus are extremely rare in domestic mammals.

Leiomyoma. Leiomyomas are benign, firm, tan, nodular tumors of the myometrium. They occur most frequently in the bitch, queen, and cow. The tumors consist of interwoven bundles of smooth muscle cells (Fig. 11.14). Collagen fibers are often interspersed with the neoplastic muscle cells. Tumors composed of smooth muscle and fibrous tissue are often referred to as fibroids. Bloom (1954) stated that "The leiomyoma represents a neoplastic proliferation of smooth muscle cells, while the fibrous connective tissue reaction is secondary." Central areas of necrosis may be present in large neoplasms.

I have seen uterine leiomyomas in 27 dogs, 12 cats, 8 cows, and 1 pig. Dogs with uterine leiomyomas often have concurrent tumors in the vagina. Leiomyomas are frequently multiple in the dog and the cat and usually single in the mare and the cow. Most of the large leiomyomas in the bovine uterus occur in the distal portion of one uterine horn or in the body of the uterus. These neoplasms must be differentiated clinically from abscesses and granulomas.

Vîtovec (1977) reported five uterine leiomyomas in a series of 120 porcine tumors that were collected over a 10-year period in South Bohemia. Arbeiter and Geigenmüller (1966) reported a 27-kg leiomyoma of the uterine wall from a cow with uterine torsion.

Leiomyosarcoma. Leiomyosarcomas are comparatively rare, but they occur in the queen, bitch, mare, cow, and goat. The tumor is more cellular, has larger nuclei than the leiomyoma, and has moderate numbers of mitotic figures.

Noordsy *et al.* (1973) reported a leiomyosarcoma of the uterus in an 8-year-old Holstein cow. Per rectal palpation revealed a 15- to 20-cm, somewhat elongated, soft mass in the uterus. An exploratory laparotomy revealed the presence of a thick-walled mass with a necrotic center. The mass had increased in size by several weeks later. A specimen was obtained for biopsy, and the mass was diagnosed as a leiomyosarcoma. The cow became debilitated and was killed 2 months later. A neoplasm was present in the dorsal uterine wall and was loosely attached to the pelvic bones. The uterus and neoplasm weighed 75 kg. Metastatic lesions were present in the omentum, diaphragm, peritoneum, mesenteric lymph nodes, liver, kidney, forestomachs, lungs, mediastinal lymph nodes, parietal pleura, and myocardium. The tumor cells were spindle-shaped and "were arranged in a criss-cross or lattice pattern." The nuclei were large, vesiculate, and round to elongated. Moderate numbers of mitotic figures were present, and tumor thrombi were found in blood vessels.

Ryan (1980) reported a uterine leiomyosarcoma from a 7-year-old Saanen doe. The goat collapsed suddenly and died. The mucous membranes were pale and about 1 liter of "dark red fluid and a large current-jelly clot" were present in the abdominal cavity. A 1.5-cm circular rent was present in the uterine wall and was "surrounded by a broad-based multilobulated rubbery-white mass originating from the dorsum of the uterine body and extending into the lumen, greatly enlarging the body of the uterus" (Ryan, 1980). The tumor extended into the broad ligaments and mesovarium, but no metastases were seen in the lymph nodes, liver, or lungs.

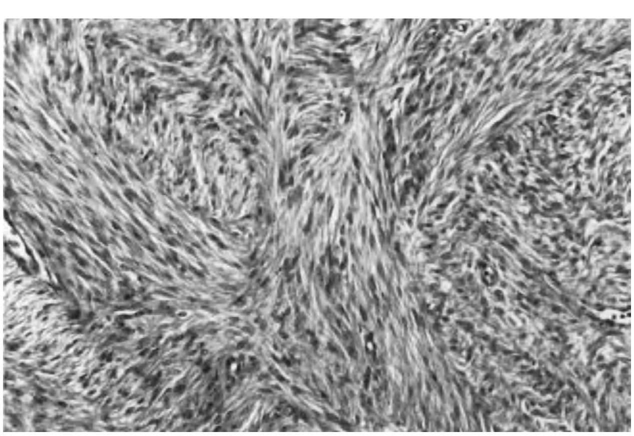

Fig. 11.14. Leiomyoma of bovine uterus. ×89. Acc. No. 19014.

Lipoma. Bloom (1954) reported that he had seen lipomas occasionally in the broad ligament of the bitch. "These are usually pedunculated, vary from 2 to 4 cm in diameter, are oval or spherical, may show areas of fat necrosis, and are enveloped by a thin fibrous capsule" (Bloom, 1954).

I examined a 25 x 16 x 7-cm lipoma of the uterine broad ligament in an aged Terrier bitch. The tumor was coarsely lobulated, soft, and fatty and occupied much of the abdominal cavity. The neoplasm was composed of mature-appearing adipose cells.

Lymphosarcoma (Malignant Lymphoma). The lymphosarcoma occurs frequently in the uterus of cattle (Smith, 1965) and occasionally in the uterus of other species of domestic mammals. The tumor presents as multiple, irregular-shaped, usually soft, gray masses (Fig. 11.15). The neoplasm usually starts in

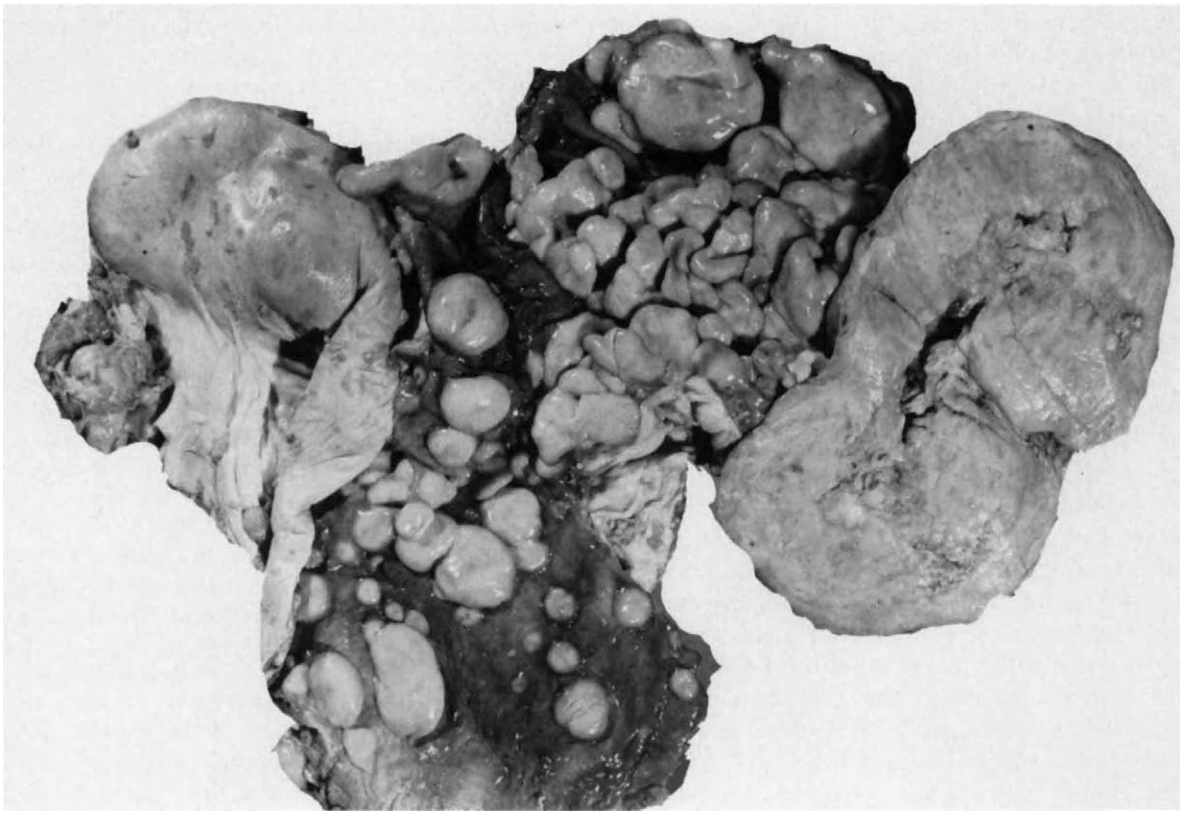

Fig. 11.15. Lymphosarcoma of equine ovary and uterus. Acc. No. 14509.

the endometrium, but occasionally commences in the myometrium. Lesions are usually present in other organs and lymph nodes.

Neufeld (1973) reviewed the literature on equine lymphosarcoma and described a case in a 15-year-old mare. The abdominal cavity contained "numerous nodular, firm, white, umbilicated masses varying in size from miliary to 10 cm in diameter." Tumors were also present in the uterus, ovary, spleen, iliac and bronchial lymph nodes, and atria and ventricles of the heart. "A mass of tumour 6 cm in diameter extended caudoventral from the base of the ear immediately posterior to the left mandible to the jugular groove, a distance of approximately 25 to 30 cm—to our knowledge, lymphoid tumours involving the uterus (of the mare) have not been described previously" (Neufeld, 1973).

One lymphosarcoma of the equine endometrium that I examined had the gross appearance of endometrial cups. Numerous circumscribed, elevated, umbilicated lesions were scattered through the endometrium (Fig. 11.16). The lesions were far more numerous and more diffusely scattered than endometrial cups. The ovaries and the sublumbar lymph nodes also contained lymphosarcoma.

The histologic features of lymphosarcomas in domestic mammals have been described by Nielsen (1969), Squire (1969), and Migaki (1969). The uterine lesions do not differ histologically from those in other locations.

Botryoid Rhabdomyosarcoma. Torbeck *et al.* (1980) reported a botryoid rhabdomyosarcoma of the uterus of a yearling Quarter Horse. The animal was examined because of a bloody vaginal discharge.

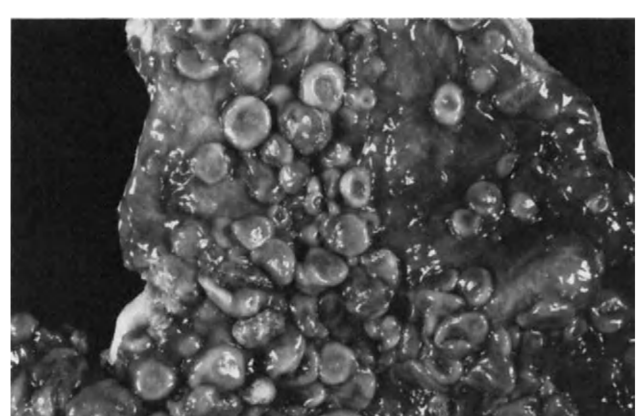

Fig. 11.16. Multiple umbilicated lesions of an equine uterine lymphosarcoma. Acc. No. 19376.

"The filly had been losing weight and the mass in the uterus had been rapidly increasing in size, being occasionally visible in the vagina."

The uterine mass was removed surgically. It weighed 18 kg and had papillary projections with the consistency of firm adipose tissue. Large areas of hemorrhage and necrosis were present. The tumor was considered to be malignant, thus the ovaries and uterus were removed. The filly died 10 days following surgery. "At necropsy, it was noted that extensive necrosis of the margin of the uterine stumps had occurred, with subsequent relaxation of the transfixing ligatures. Leakage of uterine debris had contaminated the peritoneal cavity, causing peritonitis" (Torbeck *et al.*, 1980). Metastases were not found.

"Histologically, the polypoid projections of the tumor consisted of a core myxoid tissue covered by a simple, short columnar to cuboidal epithelium. Cells in the myxoid stroma had a stellate appearance due to long, thin cytoplasmic processes" (Torbeck *et al.*, 1980). Electron microscopy revealed the presence of numerous microfilaments in the cytoplasm of the neoplastic cells and "condensation of these filaments into sarcomere-like packets was conspicuous." A diagnosis of an embryonal botryoid rhabdomyosarcoma was made on the basis of these findings.

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Chapter 12

Cervix, Vagina, and Vulva

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Bibliography

Anatomic Features

Cervix

The cervix is the most caudal part of the uterus. It provides a protective barrier against the entrance of microorganisms into the uterus. The lumen of the cervix is lined by a single layer of columnar, mucus-secreting cells that undergo changes during the estrous cycle. "The tunica propria is rich in cells and collagenous fibers and has an almost tendon-like consistency. Large amounts of this firm "cervical tissue" are also found between the bundles of the well-developed circular muscular layer; and because of its internal organization and ability to swell, it seems to play an important role in the dilation of the cervical canal" (Schummer *et al.*, 1979). The wall of the cervix contains a thinner, peripheral, longitudinal, muscular layer and a serous coat.

El-Banna and Hafez (1972) reviewed the literature on the comparative anatomy and cyclic histologic changes of the cervix and characteristics of cervical mucus of the cow, mare, ewe, sow, bitch, and queen. They stated that "During estrus, there is an increased vascularity of the cervix accompanied by congestion and edema and relaxation in the cervical muscle tone. The height of the epithelium reaches its peak during estrus and then undergoes various degrees of reduction in size and secretory activity at other phases of the cycle." The cervical canal is open during estrus and closed during metestrus and diestrus.

"The secretory activity of the cervix responds to variations in the ovarian cycle; the mucus becomes more plentiful and thinner around the time of ovulation, thereby facilitating the ascent of spermatozoa to the upper parts of the reproductive tract. At other times, only a small amount of highly viscid and tough mucus is present in the cervical canal. A direct relationship exists between the consistency of the cervical mucus and the functional activity of the corpus luteum as mucus becomes thicker and more adhesive with an increase in lutein activity" (El-Banna and Hafez, 1972).

Vagina

The vagina evolves from fusion of the caudal portions of the paramesonephric ducts and extends from the cervix to the vestibule. Most of the vagina is retroperitoneal with only a small cranial portion covered by peritoneum. A rectogenital pouch of the peritoneum extends caudally for a short distance between the vagina and the rectum. The vesicogenital pouch extends caudally somewhat further between the vagina and the bladder.

The vaginal wall consists of three layers: tunica mucosa-submucosa, tunica muscularis, and tunica adventitia or serosa. The stratified squamous epithelial lining undergoes changes during the estrous cycle. The tunica muscularis consists of a thick inner circular and a thin outer longitudinal layer of smooth muscle. The tunica adventitia contains loose connective tissue, blood vessels, nerves, and ganglia. Remnants of the mesonephric ducts persist in the ventrolateral walls of the vagina and terminate at the junction of the vagina and vestibule. The external urethral orifice is located ventrally at this junction.

Vestibule

The vestibule extends from the terminal part of the vagina to the labia of the vulva. It is lined by stratified squamous epithelium and contains the mucus-producing vestibular (Bartholin's) glands. The glands vary in occurrence, size, and number in different species.

Vulva

The vulva is the terminal part of the female reproductive tract. The right and left labia "meet dorsally in the rounded dorsal commissure and ventrally in the more pointed ventral commissure" (Schummer *et al.*, 1979). The labia of domestic mammals are homologues of the labia minora in women. "Homologues of the labia majora are not usual in the female domestic mammal, except possibly for the two cutaneous elevations, derivatives of the genital swellings, that are occasionally seen lateral to the vulva of the cat and bitch" (Schummer *et al.*, 1979). The skin of the vulva has hair follicles with soft fine hairs and numerous sebaceous and sweat glands.

The ventral commissure of the vulva encloses the clitoris, the homologue of the penis. "The attachment and structure of the clitoris are very similar to those of the penis; the main difference being that in the female the urethra is not part of the clitoris, whereas in the male the urethra is incorporated in the penis" (Schummer *et al.*, 1979).

Cow

Edwards (1965) reported that the average measurements of the cervix in European cattle breeds were 6.58 cm long × 2.84 cm wide in nonpregnant heifers and 7.75 cm long × 3.75 cm wide in nonpregnant cows. The cervix increased in size in pregnant cows from 8.82 × 4.01 cm at 1 to 3 months of pregnancy to 14.38 × 4.73 cm during the last 3 months of gestation. Some fertile zebu cows have a much larger cervix.

The bovine cervix has four thick transverse folds (plica circulares, rings). The transverse folds increase in height in a craniocaudal direction and overlap, forming a spiral canal. The caudal end of the cervix projects into the vagina for 3 to 6 cm.

Wrobel (1971) reported that the mucosa of the bovine cervix "has longitudinal primary folds running in a cranio-caudal direction and also secondary and tertiary folds. The tertiary longitudinal folds show three different epithelial regions: the ridge of the fold, its lateral walls, and the area of crypts between adjacent tertiary folds. Cyclical changes in the epithelium are most marked in the lateral walls and the ridge." The epithelial cells "are tallest in pro-oestrus and oestrus and shortest in late metoestrus and early dioestrus."

The vagina is approximately 25 to 30 cm long in nonpregnant cows and is somewhat longer in pregnant animals. Drennan and Macpherson (1966) found that the mean length of the vagina was 23.57 cm in a group of 300 15- to 30-month-old crossbred beef heifers. The length of the vagina was measured from the external cervical os to the ventral commissure of the vulva.

Scorgie and Ottaway (1942) reported the presence of annular or circular folds in the vagina of the cow. They stated that the folds "are situated in the walls of the anterior part of the vagina and form a series of complete rings round the organ. Usually four to six folds are present. In normal animals the first fold is situated at a distance of some 9 to 11 inches from the vulval orifice (labia), and the succeeding rings are about 1/2 to 1 inch apart in the living animal. The last fold is approximately 1 inch from the outer lip of the cervix." Constriction of the muscular bands in the live animal may cause the examiner to confuse the bands with the cervix in some cows.

Remnants of the mesonephric ducts (Gartner's ducts) are visible in the vaginal wall. They are located ventrolaterally near the cervix and converge ventrally toward the vaginal-vestibular junction where they terminate. Openings to the ducts are sometimes evident at this junction.

The cow has one pair of major vestibular glands (Bartholin's glands), which are 2 to 3 cm in diameter and somewhat flattened. Their ducts open into small mucosal recesses on the lateral walls of the vestibule, a short distance caudal to the junction of the vestibule and vagina.

Ewe and Doe (Goat)

"The cervix of the goat has up to eight transverse folds, while that of the ewe in addition to two transverse folds had five to six hard prominences arranged longitudinally" (Schummer *et al.*, 1979). According to Lyngset (1968), the average length of the cervix in nonpregnant does is 5.73 cm. Abusineina (1969b) reported that "The mean length, width and weight of the cervix uteri of sheep increased with advancing pregnancy. Length and weight increased most markedly when crown–rump length of the foetus exceeded 40 cm." The mean length of the cervix was 7.75 cm when the fetal crown–rump measurement ranged up to 10 cm. The range in cervical length was 5.7 to 10 cm. In uteri containing fetuses with 40- to 50-cm crown–rump lengths, the mean length of the cervix was 12.98 cm with a range of 11.5 to 15 cm. In regard to the ovine cervix, Bunch and Ellsworth (1981) reported that "The second fold is eccentric to the other concentric folds and presents a physical barrier to the passage of a straight instrument, a phenomenon that has prevented the use of deep cervical or uterine artificial insemination."

Dun (1955) classified the cervices from 112 slaughtered Merino ewes as follows: "Type 1: A single teat-shaped cervical papilla protruded into the vagina in 48% of the 45 maiden ewes. The cervical opening was located immediately ventral to the base of the papilla. Type 2: In 27% there was a small cylindrical or teat-shaped papilla as in type 1, but the opening was visible as a horizontally placed slit on the apex of the teat. Type 3: No papilla was present in 17%. There was a slit-like opening in the wall of the anterior vagina. . . . Type 4: In 8% the os uteri faced in any direction and was found variably placed on a mound of tissue on the floor of the anterior vagina." Pregnancy and parturition increased the size and complexity of the cervical papillae. In older animals, the papilla of the type 1 cervix was enlarged, broad, and "shelf-like." "Those papillae with a central opening appear to be split by parturition into several tongue-like projections with the opening in between. Parturition also splits the annular folds lining the cervical canal with the formation of variously shaped tags which project out the enlarged cervical opening" (Dun, 1955). It might be questionable whether there is actual splitting of the papillae and folds or whether polypoid formations develop and enlarge as a result of multiple pregnancies.

"Occasionally, major and minor vestibular glands are present in the vestibule of the ewe, but never in the goat. The labia of the vulva are not very prominent, and at the ventral commissure taper to a point which is larger in the ewe. The body of the clitoris is short in both species, and the tip of the glans projects only slightly from the fossa clitoridis" (Schummer *et al.*, 1979).

Mare

The cervix of the mare is 5 to 7.5 cm long and 3.5 to 4 cm wide. The caudal portion projects into the vaginal lumen. The mare, in contrast to other species of domestic mammals, does not have transverse cervical folds. Longitudinal mucosal folds, which are continuations of the uterine folds, are present. According to Ginther (1979), "a fold of the cervix extends onto the floor of the vagina as a frenulum." Up to four small diverticulae are present in the midventral portion of the mucosa in some mares. The diverticulae are not seen unless the mucosa between the cervical folds is examined carefully. These structures were brought to my attention by Virginia E. Osborne of the University of Sydney, Australia.

The caudal extremity of the vagina "is marked by a prominent transverse fold which often lies over the urethral orifice. The fold in young mares is more distinct, forming the hymen that restricts the entrance to the vagina" (Ginther, 1979).

The mare has minor vestibular glands. "They can be detected by their crater-like small openings arranged in two ventral and two dorsolateral rows" (Schummer *et al.*, 1979). The four linear rows of openings converge toward the clitoris. The mare has a large glans clitoris (about 2.5 cm in diameter) that occupies a deep fossa clitoridis.

Sow

Cowan and Macpherson (1966) examined the reproductive tracts from 32 puberal gilts and 187 sows. They found that the mean length of the cervix in gilts was 17.37 cm and 20.47 cm in sows. The vaginal lengths were 15.15 cm for gilts and 19.84 cm for sows. The vaginal length was measured from the external cervical os to the vulvar opening.

Smith and Nalbandov (1958) reported that the porcine cervix consists of "two distinct anatomical portions, the uterine portion, which is up to 4 to 5 cm long, and the vaginal portion, which is approximately 10 to 12 cm in length. Both portions have annular rings and are histologically similar." They found that the uterine portion of the cervix was constricted throughout the estrous cycle and that the vaginal portion was constricted during estrus and relaxed during midcycle. The cervix of the other species of domestic animals relaxes and the cervical canal dilates during estrus. "The anatomical peculiarities of the penis in relation to the annular rings of the vaginal cervix, and actual observations made during mating, make it appear probable that the penis is actually gripped by the annular rings and that ejaculation does not occur until such a union has occurred" (Smith and Nalbandov, 1958). Rigby (1967) suggested that the rigidity of the porcine cervix during estrus may be due to edema rather than to muscular contraction or vascular engorgement.

The mucous membrane of the porcine vagina is arranged in high longitudinal folds. "At the junction with the vestibule, in the virginal animal, is an annular fold 1 to 3 mm high, homologous to the hymen" (Schummer *et al.,* 1979).

Bal and Getty (1972) described the vaginal histology of pigs from birth to 8 years of age. A subepithelial elastic area appeared in the vaginal mucosa after 1 year of age. "Above 2 years of age, epithelial folds or invaginations were seen in the tunica mucosa as microcysts or cell nests." The invaginated epithelial folds appeared to increase with advancing age and were not considered to be pathologic.

The mesonephric ducts were lined by two to three layers of stratified ciliated cuboidal epithelium in gilts below 1 year of age. Tubular outgrowths of the ducts occurred at about 2 years and increased with advancing age. They stated that "these structures somewhat resembled the collecting tubules of the medulla of the kidney" in sows over 6 years old (Bal and Getty, 1972).

Bitch

The size of the canine cervix varies according to breed and measurements have not been reported for most breeds. The cervical canal is directed caudoventrally from the uterus to the vagina. "The cervix lies diagonally across the uterovaginal junction. Its ventral border attaches to the uterine wall cranial to its dorsal attachment. Consequently, the internal orifice of the cervical canal (ostium uteri interna) is facing almost directly dorsally, whereas the external orifice (ostium uteri externum) is directed toward the vaginal floor" (Evans and Christensen, 1979). The cervical canal is about 0.5 to 1 cm in length in medium-sized breeds.

The canine vagina is relatively long and the mucous membrane forms prominent longitudinal folds. The folds become very edematous and enlarged during proestrus and estrus. Pineda *et al.* (1973) were the first to report the presence of a dorsal median postcervical fold in the vagina of the bitch. The fold "extended caudal from the edge of the vaginal portion of the cervix. The fold terminated caudally by blending into lesser dorsal longitudinal folds." They suggested that the dorsomedian postcervical fold may have a physiologic role in mating.

Two rows of minor vestibular glands are present in the ventral part of the vestibule and their ducts open on either side of a median ridge. Numerous lymph nodules are present in the vestibular mucosa. The labia of the vulva are thick and form a pointed ventral commissure.

Queen

The feline cervix protrudes into the vagina as a prominent papilla that is directed ventrocaudal. "A prominent ridge is continued from its caudodorsal side along the mid-dorsal wall of the vagina" (Reighard and Jennings, 1935). The vagina and vestibule are about 4 cm long. "The cat has major vestibular glands, about 5 mm in size, in the lateral walls of the vestibule, with small openings that can be detected in the vestibular floor" (Schummer *et al.,* 1979).

Congenital Anomalies

Minor Congenital Anomalies

Mesonephric Duct Remnants. Remnants of the mesonephric ducts are present in the cervix and vagina of all species of domestic mammals. They become cystic most frequently in cattle and occasionally in other species. Estrogen and highly chlorinated naphthalene induce squamous metaplasia of the ductal lining and cyst formation in cattle. Cystic ducts rarely occur in young heifers and thus the presence of cystic mesonephric ducts in the vagina of young animals is suggestive of highly chlorinated naphthalene poisoning (Fig. 12.1) (McEntee and Olafson, 1953).

Dorsoventral Bands at Level of Hymen. Medially located dorsoventral bands of epithelial-covered fibrous tissue are frequently present at the junction of the vestibule and vagina in virgin heifers. The bands

Fig. 12.1. Cystic mesonephric ducts in the vagina of a 6-month-old heifer with highly chlorinated naphthalene poisoning. Acc. No. 2537. (Dobberstein *et al.*, 1985.)

are usually thin and are broken during natural service or during parturition in artificially inseminated heifers. The presence of this band in a pregnant heifer indicates that she has been bred artificially.

Major Congenital Anomalies

Van Loen (1961) reviewed the literature dealing with cervical malformations in the cow, mare, sow, and bitch.

Persistence of the Medial Walls of the Paramesonephric Ducts. Major congenital anomalies occur more frequently in the cervix than in other parts of the reproductive tract, and more frequently in cattle than in other species of domestic mammals. Persistence of a portion of the medial walls of the paramesonephric ducts, which are destined to develop into cervix, results in the formation of a double cervix. The duplication of the cervical canal may be complete or partial. Incomplete duplication occurs more frequently than complete duplication and usually involves the portion of the cervix adjacent to the vagina. The persistent medial walls may extend into the vagina for a few millimeters to a few centimeters, and rarely for the entire length of the vagina.

Cow. Bissonnette (1924) studied the embryology of the bovine reproductive tract by dissecting embryos of different crown–rump (C–R) lengths. He found that the cervix is double at the 5.1- and 7.5-cm C–R stages of development while the body of the uterus and the vagina have a single lumen. The annular folds of the cervix appear at the 15-cm C–R stage.

Van Loen (1961) investigated the incidence, effect on fertility, and mode of inheritance of the double cervix condition in Meuse-Rhine-Ijssel cattle. During clinical examination, a total of 607 cases (3.7%) of double cervix were encountered among 16,375 cows. Postmortem examination of the genital tract of cows of the same breed was also done. "The incidence of duplication in different positions of the genital tract totaled 21 cases out of 301, i.e., about 7%." Concerning the effect of the defect on fertility, he concluded that it was not "a serious source of loss to breeders generally." The affected cows required an average of 1.75 inseminations per conception compared to 1.59 in the normal cows. The double cervix condition did not appear to increase the incidence of abortion, dystocia, stillbirth, or retention of the placenta. "Regarding the mode of inheritance, it is highly indicative that the predisposition to the double cervix condition is due to an autosomal dominant gene ($p = 0.17$) with incomplete penetrance ($z = 0.13$)."

Sittmann *et al.* (1961) reported a high incidence of double cervix in two closely related herds of Hereford cattle. Seventeen (12.8%) of 125 cows in one herd and 19 (6.8%) of 279 animals in the other herd were affected. They stated that "The evidence indicates that inheritance of this sex-limited defect is conditioned by a single autosomal recessive gene with low penetrance and variable expressivity. . . .The adverse effect of the double cervix condition on fertility in Hereford cows is extremely small under ordinary beef cattle management."

Although the overall adverse effect of the cervical defect on fertility is not large, individual animals may have serious problems. Difficulty may be encountered during artificial insemination if one of the cervical canals ends blindly. Conception may not occur in a cow with uterus bicorpor bicollis (uterus didelphys) if semen is deposited in the cervical canal contralateral to the ovary containing the mature follicle. Duplication of the cervix also causes dystocia in primiparous heifers, especially if more than one transverse cervical fold is duplicated.

Sow. Teige (1957) examined the reproductive organs from 9250 gilts and 476 sows and found that the incidence of the double cervix condition was very low. Anomalies were found only in gilts. Four (0.043%) among 7107 had uterus bicorpor bicollis (uterus didelphys) and 2 (0.093%) among 2143 gilts had uterus bicorpor bicollis and a double vagina. The vagina was discarded and thus not examined from the first series of 7107 specimens.

Einarsson and Gustafsson (1970) examined the reproductive organs from 1000 gilts. They found one uterus didelphys and double vagina, one total duplication of vagina and cervix, one total duplication of vagina, three partial duplications of vagina and cervix, two partial duplications of cervix, one blind vagina at the border of the vestibule, and 41 dorsoventral bands at the junction of the vestibule and vagina.

Morris (1954) reported a triple cervix in a gilt that had been in labor for about 12 hours, "when she finally produced five living piglets and one stillborn. She did not cleanse normally and odd pieces of decomposed tissue and mucous continued to be passed for same time." Fetal bones were passed "after a day or two" and the gilt "milked poorly" and had an elevated temperature. The cervix was thick and the caudal portion protruded into the vagina. Three cervical canals extended through the cervix. "The 'body' of the uterus possessed two separate cavities, two cervical canals passing into the cavity on the right and one canal into the cavity on the left."

Ewe. Single cases of double cervices in the ewe have been reported by Schmaltz (1911), Curson and Belonje (1934), and Dutt (1954). Gustafsson and Holmberg (1966) examined the reproductive organs from 502 slaughter ewes. They found one genital tract with duplication of the cervix and vagina and four tracts with duplication of the caudal portion of the vagina.

Mare. Macrae (1935) diagnosed partial duplication of the caudal portion of the cervix in a 4-year-old Clydesdale mare that had been bred several times and failed to conceive.

Cervical Agenesis. I have seen agenesis of the cervix in the bitch and queen. The uterine body ends blindly and the uterus becomes distended with fluid. Membranous tissue separates the uterus from the vagina. Schlotthauer and Zollman (1956) recorded a case in a Shetland pony.

Cervical Aplasia. Teige (1957) found 10 cases of aplasia of the uterine body, cervix, and vagina in a series of 9250 gilts.

Cervical Hypoplasia

Cow. I have examined the reproductive tracts from a few Holstein-Friesian heifers with short cervices and a deficiency or a complete lack of transverse cervical folds. One 3-year-old heifer had been bred nine times without conceiving. Her cervix was 4.7 cm long and had only partial development of the two distal transverse folds on the right side. The rest of the cervical mucosa was smooth. The heifer had chronic endometritis and discharged exudate from the uterus.

Mare. Blanchard *et al.* (1982) reported a case of cervical hypoplasia in a 2-year-old Thoroughbred filly that had severe, persistent pneumovagina. "Visual examination through a speculum revealed the cervix to be short (1 to 1.5 cm) and dilated, allowing air to be aspirated into the uterus."

Cervical Atresia. Atresia of the internal cervical os may occur alone or in combination with other congenital defects of the reproductive tract in cattle. The opening between the cervix and the body of the uterus may be so small that mucus accumulates in the uterus. I have seen the defect as a single malformation in Holstein-Friesian cattle. Peterson *et al.* (1966) reported the condition in Jersey and milking Shorthorn type cattle in Australia. The affected animals also had other congenital defects of the cervix.

Tortuous Cervical Canal. Tortuous cervical canals occur predominantly in the Holstein-Friesian breed. The canal may be so crooked that it is impossible to pass an insemination pipette (Fig. 12.2). Affected heifers fail to conceive and the cervical lumen becomes filled with thick, rubbery mucus similar to that which accumulates during pregnancy. Mucometra develops when the lumen is thus blocked. If the condition is diagnosed early, the cervix can be bypassed by making an incision in the dorsolateral wall of the cranial vagina and depositing semen near the ovary at the proper time of the estrous cycle. These heifers will conceive but the procedure is not recommended except for experimental studies. The condition is probably inherited since the incidence varies according to breed.

Cervical Diverticulum and Sacculation of the Cervical Canal. Peterson *et al.* (1966) reported that single or multiple defects of the paramesonephric duct system were found following slaughter in 16 (8 milking Shorthorns and 8 Jerseys) of 25 infertile heifers. Ten had segmental aplasia of the uterus and 10 had sacculation and/or diverticula of the cervical canal. Some had single defects and others had multiple anomalies.

The dilation (sacculation) of the cervical canal (Fig. 12.3) "was always near the anterior end of the cervix, usually within a few millimeters of the internal os" (Peterson *et al.*, 1966). The dilated area "was more or less spherical and symmetrical about the longitudinal axis of the canal; its lining was mostly smooth and

Fig. 12.2. Tortuous cervical canal from a Holstein-Friesian heifer. The cervix contained tenacious mucus and the uterus was distended with watery fluid. Acc. No. 18015.

Fig. 12.3. Constriction of third cervical ring and dilated area between third and fourth rings. Hemorrhage on third ring was due to attempted passage of a pipette prior to slaughter. Acc. No. 10315. (Figures 12.3 and 12.4 from Jubb and Kennedy, 1970.)

free of permanent folds." The cervical diverticula (Fig. 12.4) "were situated dorsal or dorsolateral to the cervical canal, with which they communicated directly through a wide opening. . . . The sacculations varied from 1 to 4 cm in diameter, and the diverticula were 1 to 2 cm deep." The diverticula and dilatations were filled with mucus, usually of a thick rubbery consistency.

In another group of 54 heifers, 11 (20%) were found to be infertile after six services. "Seven (13%) had a cervical sacculation or diverticulum of sufficient size to be the probable cause of the infertility" (Peterson *et al.*, 1966).

Dorsal diverticula were found in 4 (4.6%) of 88 fertile cows that had had one to four calves. The largest diverticulum was 1.2 cm in diameter and the rest were much smaller than those found in infertile heifers. They concluded that the developmental defects "are frequent in heifers and significant in infertility." The etiology of the condition was not determined.

Constriction of the Vagina. Maxwell (1977) reported the occurrence of constriction of the vagina in Merino ewes. The defect was located "at about the junction of the cranial and middle third of the vagina." The incidence of the defect and the effect on fertility were investigated in 12 flocks. "The overall incidence of the constriction was 11% with a range from 2% to 27%." Ewes with the defect "exhibited inferior reproductive capacity; fewer ewes lambed and of those that did fewer reared their lambs. A higher lamb mortality was recorded in lambs born to such ewes."

Segmental Aplasia of the Vagina (Transverse Vaginal Septum). Various degrees of aplasia of the vagina and uterus have been reported in Shorthorn and Swedish-Friesian cattle (Spriggs, 1946; Nordlund, 1956).

Wadsworth *et al.* (1978) reported segmental aplasia of the vaginal mucosa in three purebred Beagle

Fig. 12.4. Two dorsal diverticula in bovine cervix. Acc. No. 10316.

bitches with normal-appearing external genitalia. "Internally, the lumina of the midvaginas (approximately 10 cm cranial to the vulva) were found to be imperforate and atonic due to the presence of mucoid material." The rest of the genitourinary tract was normal.

Gee *et al.* (1977) reported a case of segmental aplasia of the vagina in a 14-month-old Bull Mastiff bitch with a 7-month history of intermittent vaginitis. The clinical problem started at about the time of the first estrus. The vulva was swollen and discharged a mucopurulent exudate. Exploratory laparotomy revealed the presence of green serous fluid in the uterus from which bacterial cultures were negative. About 75 ml of fluid was aspirated from the portion of the vagina caudal to the patent cervix. The vagina was cut cranial and caudal to the obstruction and the cut ends were anastomosed end to end. The bitch conceived on her second postoperative estrus and whelped eight puppies. Apparently, the female offspring were not examined thoroughly but it was stated that they did not have a vulvar discharge.

Persistent Hymen. A complete hymen is rare in all domestic mammals except the mare. It occurs occasionally in cows as a single lesion (Fig. 12.5) or in association with segmental aplasia of the uterus. A complete hymen is the most common major congenital defect of the tubular genital system of the mare; the condition can be corrected by surgery. It is not known if the defect is inherited.

Vaginal and Rectal Constriction. Hull *et al.* (1940) reported that many of the 22 daughters of a Jersey bull that were raised to maturity had a narrow vulva and vagina. The rectum and anus were constricted in most of the heifers. Leipold and Saperstein (1975) reported that "Three Jersey herds had a total of 14 cows with constriction of the anorectal area and the vagina. Maternal and paternal lines of all affected

Fig. 12.5. Reproductive tract from a white Shorthorn heifer with an imperforate hymen. The vagina, cervix, and uterus were distended with fluid. Acc. No. 889.

cows traced to a common ancestor." The defect appears to be due to an autosomal recessive gene (Leipold *et al.*, 1981). It was impossible to insert the forearm into the rectum in many cases. "Affected cows had such nonelastic vaginas that caesarium section or episiotomy was required for first calving and subsequent calvings were difficult." The rectum was narrow at the anorectal junction and the vagina had a narrow diameter close to the vulva.

Rectovestibular and Rectovaginal Fistulas (Atresia Ani Sinourogenitalis, Cloaca). During embryonic development, the urorectal septum may fail to develop, resulting in a persistent cloaca. The fistula from the rectum generally opens into the vestibule at the junction between the vestibule and vagina and feces are discharged through the vulva. The fistula opens less frequently into the vagina or uterus (Nieberle and Cohrs, 1967). I have seen rectovestibular fistulas in the pig (Fig. 12.6) and goat (Fig. 12.7).

Fig. 12.6. Rectovestibular fistula in a 6-month-old pig. Acc. No. 679.

Fig. 12.7. Rectovestibular fistula in a newborn Saanen goat. The colon was distended with feces. Acc. No. 16349.

Anovaginal Cleft. Single cases of anovaginal clefts have been reported in a Miniature Poodle and a German Shepherd pup (Wilson and Clifford, 1971; Burke and Smith, 1975). "The mucosal surface of the anus and vagina were continuous along the perineal raphe. When the labia of the vulva were separated, an enlarged clitoris was exposed in the fossa. The urethral tubercle and orifice were not visible" (Wilson and Clifford, 1971). The cranial portion of the vagina was normal and the defects were repaired surgically in both dogs. It is not known whether this is a genetic defect.

Ectopic Mammary Gland in the Vulvar Labia. The presence of ectopic mammary tissue has been reported in the goat (Lesbouyries and Drieux, 1945; Kulkarni and Marudwar, 1972; Smith, 1980). Large, soft to firm, oval swellings appear in the labia of vulva during late gestation. They extend from the level of the ventral commissure of the vulva to the anus. The swellings regress at the end of the lactation period. The tissue resembles normal lactating gland with the exception that the ducts are widely distended with milk.

Vestibular Wattle. I have seen three young heifer calves with an elongated spherical mass, 4 to 5 cm long and 0.5 to 0.8 cm in diameter, attached to the mucosa of the vestibule adjacent to the dorsal commissure of the vulva. Roberts (1971) referred to this anomaly as a wattle. Pritchett (1941) surgically removed two wattles from the vestibule of a 3-month-old Jersey calf and called them "vaginal papillomas." The owner noticed the lesion when the calf was about 3 weeks old. From the description of the case it appears that the lesion was present at birth.

Vascular Lesions

Hyperemia and Edema

Hyperemia and edema of the cervix, vagina, and vulva occur during estrus. In regard to the mare, Hughes *et al.* (1975) stated that "Characteristic visual and palpable changes were noted in the cervix during oestrus beginning with a progressive softening and relaxation just before the onset of heat. There was a color change from white to red, [and] cervical oedema increased. . . . These changes were greatest near ovulation but alone were not an accurate indication of the time of ovulation."

During anestrus the canine vagina has multiple, shallow, longitudinal folds. During proestrus and estrus, edema of the vagina results in marked enlargement of the longitudinal folds with the formation of cross sulci. The edema subsides during metestrus.

Multifocal areas of proliferation of fibrous tissue develop in the canine vagina as a consequence of repeated episodes of edema. These focal fibrotic lesions gradually protrude into the vaginal lumen and become pedunculated, forming fibromatous polyps. The largest lesion is often on the floor of the vagina just cranial to the urethral orifice. Large polyps protrude between the vulvar labia and become ulcerated.

Mycotoxic Hyperestrogenism (Zearalenone Toxicosis)

Swine. Farmers in the Corn Belt of the United States complained of "false heat" and infertility in the swine herds in the early 1900s (Mirocha *et al.*, 1977). The feeding of moldy corn to 25- to 40-pound gilts resulted in the development of vulvar edema within 2 to 4 days (Buxton, 1927; McNutt *et al.*, 1928). The disease occurs in pigs of all ages, including newborn piglets, but most frequently in gilts from 6 weeks to 7 months of age. The first change to be noted is swelling of the vulva similar to that of estrus, but the enlargement continues until the labia are very smooth and firm. The mucosa of the vestibule and vagina protrudes through the lips of the vulva. The prolapsed tissue becomes congested, ulcerated, hemorrhagic, and infected. Prolapse of the rectum occurs in 5 to 10% of the cases, while prolapse of the vagina may occur in 30% (McNutt *et al.*, 1928). Death occurs only in cases of prolapse and then from secondary causes such as cystitis, uremia, or septicemia. The mammary glands become enlarged in some affected gilts.

Stob *et al.* (1962) and Christensen *et al.* (1965) isolated an estrogenic mycotoxin (zearalenone, F-2 mycotoxin) from *Fusarium graminearum (Giberella zeae)*, which grows in stored, high-moisture grain. A concentration of 1 to 5 ppm of zearalenone in the feed causes clinical signs of hyperestrogenism in swine (Loncarevic *et al.*, 1977). Ten-week-old gilts that were fed zearalenone developed vulvar edema, ductal hyperplasia of the mammary glands, edema, and hyperplasia of the uterus and squamous metaplasia of the cervix and vagina (Kurtz *et al.*, 1969). Chang *et al.* (1979) reported that the feeding of 95% purified zearalenone to multiparous sows induced a number of reproductive disorders, including infertility, small litters, small piglets, juvenile hyperestrogenism, and possibly fetal absorptions. The clinical signs of infertility were nymphomania or pseudopregnancy. The nymphomaniac sows had ovarian atrophy but did not have obvious changes in the external genitalia. The pseudopregnant sows had multiple corpora lutea with a life span equal to or longer than that of a normal gestation period. Squamous metaplasia was present in the ductal epithelium of the mammary glands and in the mucosa of the uterine tubes, uterus, cervix, and vagina.

Cattle. Ványi *et al.* (1974) reported the occurrence of mycotoxic hyperestrogenism in cattle. Five to 75 ppm of zearalenone were found in the feed of cows that had swelling of the vulva, a drop in milk production, and a lack of appetite. Abortions did not occur. Bloomquist *et al.* (1982) reported the occurrence of mammary gland enlargement in prepubertal dairy heifers that were fed moldy corn.

I have seen heifers develop prolapse of the vagina and rectum after prolonged exposure to zearalenone. The histologic lesions consisted of squamous metaplasia of the ducts of the vestibular glands and the mesonephric duct remnants and hyperplasia of the mammary gland ducts.

Varicose Veins

Varicose veins are present at the junction of the vestibule and vagina of some mature and aged mares. The distended tortuous veins protrude above the mucosal surface and are ruptured during natural breeding, resulting in a modest amount of hemorrhage. The hemorrhage does not interfere with fertility.

Inflammatory Lesions

Cervix

Cervicitis does not occur as a single entity but accompanies vaginitis and/or endometritis. All animals with endometritis have some degree of cervicitis but the inflammatory reaction is usually less severe in the cervix than in the endometrium. Most inflammatory reactions due to infection are superficial with the exception of those due to necrobacillosis and tuberculosis.

Purulent cervicitis develops occasionally in the bitch following ovariohysterectomy. A watery, purulent, or hemorrhagic vulvar discharge may persist for months or even years subsequent to surgery. If the uterus is removed cranial to the uterine body, the remnant may become greatly distended with exudate. The condition can be prevented during ovariohysterectomy by removing the cervix with the rest of the reproductive tract (Badinand, 1973).

Vagina and Vulva

Most animals have inflammatory cells in the subepithelial tissue of the vagina and vestibule owing to the presence of microbial flora in the lumina of these structures. The inflammatory lesions are often mild because of the protective function of the stratified squamous epithelial lining.

Vestibular Lymphocytic Follicles (Granular Venereal Disease)

Nodules of lymphocytes are present in the subepithelial tissue of the vestibule in all species of domestic mammals. They are arranged in parallel longitudinal rows in cattle and are especially numerous and randomly distributed around the clitoris. Irritation of the vestibular mucosa by chemical or microbial agents induces hyperplasia and hyperemia of the lymphocytic nodules. This condition is commonly referred to as "granular venereal disease." The concept that this is a specific disease is erroneous. It is not a manifestation of a specific disease but merely a sign of irritation of the vestibular mucosa.

Many different agents cause hyperplasia of lymphoid follicles in the vestibule. Singh *et al.* (1974, 1975) reported that "granular vulvovaginitis (GVV) was experimentally produced in female kids by topical application of *Mycoplasma agalactiae* on scarified vulvar mucosa." Doig *et al.* (1979) reported bovine granular vulvitis associated with *Ureaplasma* infection: "The acute form of the disease was characterized by a purulent vulvar discharge, an inflamed hyperemic vulvar mucosa and varying degrees of granularity. In the chronic form, there was an absence of a purulent discharge and a gradual decline in the severity of the hyperemia and granularity. Epithelial inclusion cysts were observed in approximately 10% of affected cows."

Bovine Herpes-1 Infection (Bläschenausschlag, Vesicular Venereal Disease, Coital Vesicular Exanthema, Pustular Vulvovaginitis, Infectious Bovine Rhinotracheitis-Infectious Pustular Vulvovaginitis, IBR-IPV)

Bovine herpes-1 virus is the cause of a contagious bovine disease that is transmitted by natural service, artificial insemination, mechanical means, and close contact. The vestibular lesions are not as severe following artificial insemination with contaminated semen as occurs during natural service to an infected bull (Kendrick and McEntee, 1967).

Kendrick *et al.* (1958) reported the clinical manifestations of the disease in a field outbreak and described the clinical signs and lesions in experimentally induced disease in virgin heifers. The naturally infected herd consisted of 90 dairy cows held in conventional stanchions with heads facing out. "The local veterinarian was called two days prior to our visit to examine a cow that was treading with the hind feet, switching the tail, and urinating frequently. . . . On our examination we found two cows with swelling of the vulva that caused them to hold the tail to one side. . . . Except for the two animals with swelling of the vulva, the external clinical signs were mild or completely lacking" (Kendrick *et al.*, 1958). The two animals with vulvar edema had a bright red vestibular mucosa that was streaked with a tenacious exudate. Plaques of gray-white exudate were attached to the mucosa. "Only about 15 animals were examined and of these it was estimated that about 75% were affected" (Kendrick *et al.*, 1958). One cow had "numerous closely spaced, round, white areas approximately 0.5 mm in diameter" in the vestibular mucosa. Others had a few raised areas about 2 mm in diameter in the vestibule. All the affected animals exhibited signs of pain when the vulva was touched. Exudate was present in the vagina of the more severely affected animals.

"The disease subsided in about 10 days. Several animals continued to have a vaginal discharge for about 6 weeks" (Kendrick *et al.*, 1958). Breeding by natural service was resumed about 3 weeks after the outbreak was recognized. Fertility was normal and abortion did not occur.

Virus was isolated from the exudate from two cows and the isolate was used to infect nine virgin heifers. Three sites of inoculation were used; vulvar (three heifers), vulvar and vaginal (two heifers), and vulvar, vaginal, and uterine (four heifers). Necropsies were conducted at 24, 48, 72, and 144 hours and 40 days postinoculation.

The temperature was elevated on the second day and the fever persisted for 3 to 7 days in most of the heifers. The temperature ranged from 104°F to 106.8°F. "There was a slight, but recognizable, sluggishness and a decrease in appetite. Many of the heifers had a slight serous nasal discharge, and two animals had a slight purulent discharge from the eyes" (Kendrick *et al.*, 1958). The vulva became slightly to moderately swollen and a small amount of thick yellow exudate was present on the ventral commissure.

Two-mm hemorrhages were present in the lymphoid follicles of the vestibule within 12 hours postinoculation. Twenty-four hours after inoculation many white areas about 0.5 mm in diameter were present in the mucosa. "On the second day, small white pustules which were approximately 2 mm in diameter appeared and the entire mucosa was uniform bright red. The pustules were soft and moist with a raised edge and a depressed center. . . .The pustules tended to form over the lymphatic follicles and this resulted in the formation of rows of this lesion in some animals" (Fig. 12.8) (Kendrick *et al.*, 1958). Pain was evident when the vulva was examined and some heifers "held the tail up constantly and would strain for several minutes after urinating." During the next few days, many of the pustules coalesced to form large areas of ulceration covered by fibrinous exudate. "The small circular areas had completely healed by eight days, whereas the larger lesions required 11 days to heal completely."

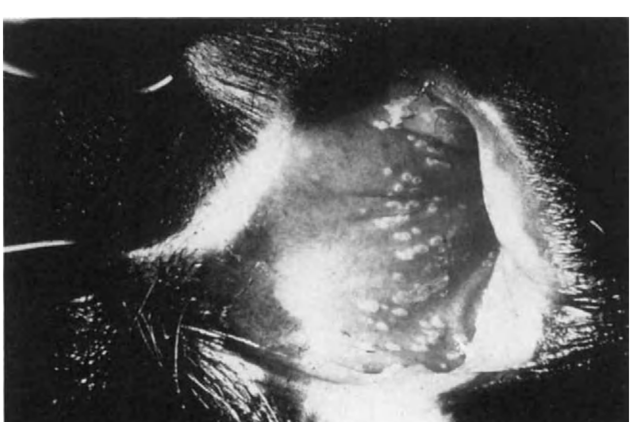

Fig. 12.8. Eroded pustules due to bovine herpes-1 infection in bovine vestibule. Lesions were present at 48 hours postinoculation. Acc. No. 4300. (Kendrick and McEntee, 1958.)

"In those animals inoculated in the vulva, changes in the vaginal mucosa were absent or limited to a slight reddening. . . .The vaginal inoculation produced a vaginitis of increasing severity according to the time post-inoculation" (Kendrick *et al.*, 1958). The mucosa was red in animals killed at 24 to 72 hours. Numerous areas of ulceration were present in those killed at 144 hours. Straw-colored fluid and exudate were present in the vaginal lumen. One heifer had extensive scarring of the vaginal mucosa at 40 days.

Intranuclear inclusions and necrosis of vestibular and vaginal epithelium were present at 24 hours postinoculation and for the next few days. A soft fixative such as 10% formalin is unsatisfactory for demonstrating the inclusions in stained tissues; a hard fixative such as Bouin's solution should be used. The lesions in the vestibular mucosa occurred predominantly over lymphatic follicles. Hemorrhage occurred in the follicles and the overlying connective tissue became necrotic. Pustules were present in the areas of epithelial necrosis at 48 hours. Within a short time, these lesions progressed to ulcers. Vesicles did not develop. Thus, the previously used term for the disease—vesicular venereal disease—was discarded in favor of pustular vulvovaginitis. The inclusions adjacent to the pustules and ulcers consisted of a homogeneous light-blue-staining material that filled the nucleus. The more peripherally affected cells contained round to oval eosinophilic inclusions with margination of chromatin. Numerous neutrophils were present in the blood vessels surrounding the follicles. "The lymph vessels contained neutrophils, lymphocytes, macrophages, and some degenerating cells. . . . Lymphocytes accumulated around the follicle in such numbers that it was impossible to recognize the sharp boundaries that normally characterize these structures" (Kendrick *et al.*, 1958). Necrotizing endometritis and cervicitis developed in heifers that received intrauterine inoculation of virus.

Infectious Bovine Cervicovaginitis and Epididymitis (Epivag, Infectious Bovine Infertility)

A severe type of vaginitis and epididymitis was recognized in Kenya in 1927 (Hudson, 1949) and was subsequently reported from South Africa (Van Rensburg, 1949). European breeds of cattle appear to be more susceptible to the disease than indigenous zebu cattle. Hudson stated that "during the active stage of infection in cows and heifers, there is present in the vagina a mucoid exudate resembling egg-white in consistency, but opaque and yellow in colour. . . . Discharge from the vulva soils the tail opposite the lower commissure and is carried by the tail to the buttocks where it dries on the hairs forming dull, grey-yellow flakes resembling shellac." Red areas are present in the vagina but ulcers, vesicles, and granular lesions are not present. The exudate is odorless and consists of "strings of mucus and polymorphonuclear leukocytes. In smears, no bacteria or protozoa are detectable and, on culture, only occasional contaminants are obtained" (Hudson, 1949).

The disease has been reproduced by inoculating material from an infected epididymis into the vagina of heifers. Redness of the vagina may be present after four days. "After seven days, redness is usually marked and discharge is to be seen after eight to 17 days. When vaginal discharge is used to produce infection in heifers, the incubation period is usually shorter, both redness and discharge often being detectable after two to four days" (Hudson, 1949). Active infection "may last for two to three weeks, or up to nine months, oestrus is normal or almost so. Service during the active stage is rarely followed by conception and there is clinical evidence to suggest that by allowing service during the active stage, the duration of infection is prolonged."

Infection spreads to the uterus, uterine tubes, and peritoneal cavity. Severe salpingitis causes blockage and distention of the uterine tubes. Adhesions between the ovaries and the fimbria of the uterine tubes results in the formation of tubo-ovarian (pavilion) cysts. Adhesions may be present throughout the pelvis and in the abdominal cavity especially "between the anterior surface of the liver and the diaphragm. In rare cases a little dry, adhesive pleurisy has been found in the thorax" (Hudson, 1949).

Although the disease can be transmitted experimentally, the etiology has not been established. Theodoridis (1978) characterized 15 virus strains that had been isolated from the vagina, cotyledon, or semen from affected cattle. "The physicochemical, morphological, and certain biological characteristics of both the 12 slow-growing and the 3 IPV-IBR related virus strains employed in this study undoubtedly relate them to the family *Herpetoviridae*. However, the serological results showed that the slow-growing virus strains are not antigenically related to the 3 IPV-IBR strains" (Theodoridis, 1978). The 15 strains were not related serologically to the herpesvirus of bovine ulcerative mammilitis. "Although it has been shown that an anterior vaginitis resembling the description of the "epivag" syndrome in females can be produced by slow-growing herpesvirus strains as well as certain IPV-IBR related virus strains, it has not been possible to reproduce the epididymitis characteristic of this syndrome in bulls. . . . Much further work is indicated before conclusions can be made about the role of herpesviruses in the aetiology of 'epivag.' " (Theodoridis, 1978).

Catarrhal Bovine Vaginitis

Catarrhal vaginitis, presumably of viral etiology, has been reported in cattle from South Africa, England, New Zealand, and California (McIntosh *et al.*, 1954; Millar, 1955; McClure, 1956; Kendrick *et al.*, 1956). Although enteroviruses have been isolated from cattle with vaginitis, it is not clear whether the isolates were the cause of the disease or were merely contaminants (Straub and Böhm, 1964; Afshar *et al.*, 1964; Straub, 1965). Kendrick attempted transmission experiments with the California isolate at the New York State Veterinary College in 1957 as part of his graduate research project. The inoculated heifers did not develop clinical signs of illness and the project was abandoned.

Equine Coital Exanthema

Studdert (1974) reviewed the literature on equine coital exanthema. It is an acute viral disease without obvious systemic signs of illness in most affected animals. The temperature, pulse, respiration, and appetite remain normal. One- to 2-mm red papules appear in the mucosa of the vestibule and vagina within 2 days after experimental infection and up to 10 days after coitus with an infected stallion. "The lesions progress rapidly to a pustular form. . . . By day 6 most primary pustular lesions appear as ulcers, some coalesced pustular areas may be up to 2 cm in diameter and 0.5 cm deep. Ulcers are demarcated by a narrow (0.2 mm) erythematous border" (Studdert, 1974). The perineal skin and the vulvar mucosa are affected. Intranuclear inclusions are present in the epithelial cells in the early areas of necrosis and in the borders of the ulcers. "In uncomplicated cases, healing is usually complete by 14 days. Where lesions have occurred on pigmented skin, their site is marked by depigmented (white) spots." Lesions may also develop on the skin about the lips and external nares and on the nasal mucosa and conjunctiva. There are three antigenically distinct types of equine herpesvirus (EHV): EHV 1 (equine rhinopneumonitis, equine abortion virus), EHV 2 (equine cytomegalovirus), and EHV 3 (equine coital exanthema virus). The EHV 1 virus has been reported to cause genital disease in the mare (Petzoldt, 1970; Turner *et al.*, 1970). The reproductive tract lesions were similar to those caused by EHV 3, but were milder and did not involve the perineal skin.

Contagious Ecthyma of Sheep and Goats (Sore Mouth, Scabby Mouth, Contagious Pustular Dermatitis, Orf)

Contagious ecthyma of sheep and goats is due to a pox virus. The disease is characterized by the sequential formation of papules, vesicles, pustules, and scabs on the skin of the lips, nostrils, eyelids, and feet, and occasionally on the skin of the vulva, udder, and prepuce. The mucosa of the mouth, forestomach, and external genitalia are also affected. The histologic lesions in the skin and mucous membranes consist of "acanthosis, ballooning degeneration of spinose cells, hyperplasia of basal cells, and edema and granulomatous inflammation of the derma. Ballooning leads to vesication and hyperplasia to nodulation" (Jensen and Swift, 1982).

Corcoran (1964) reported an outbreak in sheep in which the lesions were limited to the vulva. There was little or no involvement of the vagina and none of the affected ewes had mouth lesions.

Ulcerative Dermatosis (Lip and Leg Ulceration, Balanoposthitis, Ulcerative Vulvitis, Ovine Venereal Disease)

Ulcerative dermatosis, a contagious disease of sheep, is due to an unclassified virus. The disease is characterized by the presence of crusted ulcers on the skin of the face, feet, vulva, prepuce, and penis. The early lesion is a pustule that develops into an ulcer covered with a scab. Histologically, the lesion differs from that of contagious ecthyma in that there is a lack of epithelial hyperplasia in ulcerative dermatosis.

Ovine Posthitis and Vulvitis (Ulcerative Posthitis, Sheath-Rot, Pizzle-Rot)

Southcott and Moule (1961) reported a serious vulvitis problem in sheep grazing clover pastures in Australia. The lesion started with a reddening of the ventral portion of the vulvar labia. Small, yellow encrustations, less than 1 mm in diameter, developed in the skin of the ventral labial commissure. The glans clitoridis became enlarged and turgid, protruded from the fossa, and became ulcerated. The condition occurs more frequently in wethers and rams than in ewes. It is caused by an interaction of a high-protein diet and *Corynebacterium renale*. The diet increases the urea in the urine, and *C. renale* hydrolyzes the urea to ammonia, which severely irritates the skin and mucosa of the external genitalia (Southcott, 1965; Barajas Rojas and Biberstein, 1974).

Canine Herpesvirus Infection

Appel *et al.* (1969) reported that the intravaginal infusion of canine herpesvirus in dogs resulted in the development of a mild vaginitis. In contrast, Hill and Mare (1974) found that vaginal inoculation with another strain of the virus caused "severe vaginitis, characterized by petechial and submucosal hemorrhages and multiple lymphoid follicles." Latent vaginal infections provide a source of infection for pups during passage through the vaginal canal.

Tuberculosis

According to Nieberle and Cohrs (1967), "Tuberculosis of Gartner's (mesonephric) ducts is of frequent occurrence, generally in association with and dependent on tuberculosis of the uterus. It occurs so regularly under these conditions that tuberculosis of Gartner's ducts can be regarded as a diagnostic sign of uterine tuberculosis." One or both ducts may be affected and they are enlarged, firm and nodular. "Tuberculosis of the vaginal mucosa itself is much less frequent." Tuberculosis of the vulva and vagina may occur as a primary infection following service to a bull with genital infection (Plum, 1935).

Dourine (el Dourin, Covering Disease, Beschälseuche, Mal de Coit)

Dourine is a venereal disease of horses and other equidae caused by *Trypanosoma equiperdum* and is spread predominantly bysexual contact. It is the only form of trypanosomiasis that is transmitted directly from one mammal to another without the intervention of an insect vector. *Trypanosoma equiperdum* "differs from other mammalian trypanosomes also in the fact that it is primarily a tissue parasite, which rarely invades the blood" (Hoare, 1972). According to Hoare, "it was apparently first described by the Byzantine veterinarian Chiron (nicknamed the Centaur) in his treatise on the diseases of the horse ("*Mulomedicina Chironis*") which was written in rustic Latin and published ca. 400 A.D. . . . The disease is also mentioned in a celebrated treatise on veterinary medicine published in the XII Century in Seville by the Arab writer Ibn-al-Awan." The disease apparently originated in North Africa and then spread to other parts of Africa, and to Asia, USSR, Europe, Indonesia, and the Americas.

Williams (1889) was the first to diagnose the disease in the United States in 1886 during an outbreak in Illinois. "It is believed that it was imported from France in 1882 in an infected Percheron stallion" (Bruner and Gillespie, 1973). Dourine spread to other states before the diagnosis was made and control measures established. It was thought that the disease was eradicated in 1920 but infected animals were found in Arizona and southern California in 1941. The last place where it was known to occur in North America was on an Indian reservation in Arizona, which was released from quarantine in 1949 (Levine, 1961). Dourine has also been eradicated from western Europe and North Africa.

Edematous swelling of the vulvar labia usually occurs within 8 to 14 days after coitus with an infected stallion. Williams (1939) stated that "there is a variable discharge of dirty mucopus from the vulva. The vulvovaginal mucosa is usually swollen and irritable. The irritated state of the vulvovaginal mucosa leads to frequent urination with evidence of pain expressed by switching of the tail, stamping the feet, and rapid opening and closing of the vulvar lips." After the acute lesions subside, raised circular or oblong urticarial plaques appear in the vulvar and adjacent skin. "They are frequently called 'dollar' plaques because they have the feeling of a disk, like a silver dollar, under the skin. They vary in size from ones much smaller than a silver dollar to ones several times as large. These appear quickly and disappear within a few hours or after several days to be replaced by others" (Bruner and Gillespie, 1973). Areas of depigmentation of the affected skin and clitoris may appear within a few weeks. The later stages of the disease are characterized by anemia, paralysis of the rear limbs, inconstant fever, emaciation, and death.

Hoare (1972) reported that "The duration of the disease varies considerably: in mild cases, it may persist for 1 to 2 years and occasionally even up to 4 to 5 years; in more severe chronic cases, the disease may last only for 1 to 2 months, and exceptionally only one week. Though, as a rule, dourine is a fatal disease, infected animals sometimes recover. Furthermore, in some parts of the world, equines may be symptomless carriers of *T. equiperdum.*" Donkeys and mules are more tolerant to the infection than horses.

Mange

Brownlee (1935) reported that *Demodex* is a fairly common parasite of sheep, and that it is found most frequently in the sebaceous glands of the vulvar and preputial skin. It is found more frequently in debilitated sheep than in those in good physical condition. I have seen *Demodex* mites in the vulvar skin of the bitch as well as the ewe. Gross lesions are seldom evident, but the mites occasionally produce granulomas.

Traumatic Lesions

Coital Injuries

The penis of the bull and stallion is longer than the vagina of the cow and mare. Ordinarily, the vagina stretches during coitus but in rare instances it ruptures. This may occur when a large bull breeds a small heifer on pasture or when a cow is restrained in a breeding rack during coitus. I examined the uterus from one cow that died within a short time following rupture of the vagina. The cow was restrained in a breeding rack during service to a large bull. A 7-cm transverse rupture of the dorsal wall of the vagina was present 3.5 cm caudal to the cervix (Fig. 12.9). This was the second cow in the herd to die in this manner.

A 16-month-old Holstein-Friesian heifer was pasture bred and subsequently became bloated and developed a purulent vaginal discharge. I examined the heifer 5 months later. At this time there were extensive, firm adhesions between the rectum and uterus (Fig. 12.10). The heifer was pronounced sterile and was slaughtered. Multiple abscesses up to 2.5 cm in diameter were present in the diffuse fibrous adhesions between the rectum and the reproductive tract. Several abscesses up to 2 cm in diameter were present in both uterine horns. A transverse scar was present in the dorsolateral wall of the vagina near the cervix. Both ovaries and uterine tubes were buried in adhesions and the tubes were cystic. Numerous abscesses were present in the mesentery and liver and adhesions were present around the intestines. In summary, the perforation of the uterus by the penis of a bull may result in death due to shock or acute peritonitis or an animal may survive with diffuse chronic peritonitis.

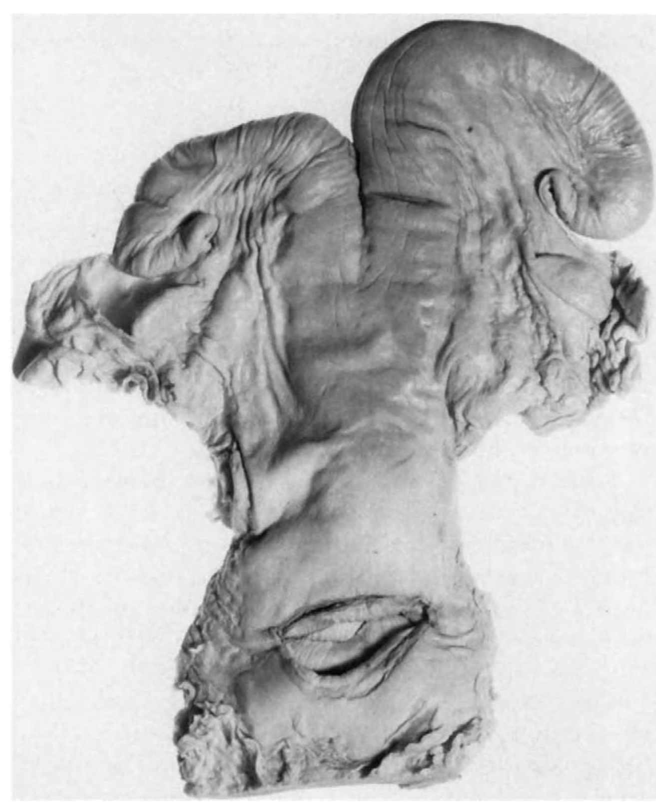

Fig. 12.9. Transverse rupture in dorsal part of cranial vagina of a cow. Acc. No. 5301.

Fig. 12.10. Dense adhesions between uterus and intestine of a heifer. The adhesions were separated before the specimen was photographed. Acc. No. 1004.

Held and Blackford (1984) reported three cases of vaginal perforation that occurred during coitus in mares. They stated that "the most consistent clinical sign of vaginal perforation is a small amount of blood escaping from the vulvar lips immediately after breeding. Secondary infection and post-traumatic swelling may cause signs of abdominal pain due to rectal impaction from abscesses or hematomas impinging on the rectum and narrowing its lumen."

Roberts (1971) reported that "in a mare with a tipped or horizontal vulva, occasionally the penis of the stallion may slide over the vulva and enter the rectum, causing a rupture of the mucosa of 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."

The vagina of various domestic mammals has been ruptured by sadists and sexual perverts forcing broom handles and other objects through the vaginal wall. It is not unusual for more than one occurrence to take place on a given property.

The penis of the bull or of the boar may occasionally pass through the urethra into the urinary bladder; it may rupture and result in acute peritonitis. If the bladder does not rupture, severe cystitis develops.

Parturient Injuries

The cervix, cranial vagina, and vestibule may be lacerated during parturition, especially in heifers calving for the first time. The ventral portion of the cervix adjacent to the uterine body is occasionally torn during parturition in dairy heifers. The lesion usually heals uneventfully, leaving only a small scar. The craniolateral wall of the vagina, adjacent to the cervix, is occasionally lacerated. Invaginated vaginal mucosa becomes sealed off, forming epithelial inclusion cysts. These may be several centimeters in diameter and may be confused with cysts of the mesonephric duct.

Laceration of the cervix during parturition is more serious in the mare than in other species of domestic mammals. Multiple longitudinal tears may occur in the mucosa and underlying tissue and result in severe scarring and adhesions that may occlude the cervical lumen.

Lacerations occur during parturition in the lateral wall of the genital tract at the junction of the vagina and vestibule in cattle (Fig. 12.11). In severe cases, the tear extends through all layers of the tubular wall. In excessively fat animals, a mass of adipose tissue protrudes into the lumen and becomes infected and covered by granulation tissue. This lesion may be confused with a neoplasm on gross examination. If tissue is taken for biopsy, a deep incision must be made into the mass to reveal the fat. The superficial part of the mass consists of proliferating fibroblasts, small blood vessels, and inflammatory cells. This granulomatous portion of the lesion may be misdiagnosed as a fibropapilloma.

Rectovaginal Fistula. Various degrees of laceration of the vagina and vulva occur during abnormal parturition in the mare. First-degree laceration involves the vaginal and vulvar mucous membranes. Second-degree tears involve the entire wall of the vagina and vulva and third-degree injury extends to include the rectum. Perineal lacerations occur most often in the primiparous mare. "Third degree perineal lacerations are due to the violence of the expulsive efforts during parturition and are associated with an abnormal condition of the mare, foal or both. The most common cause is malposture of the fetus in which one or both forelegs are over the head or neck. On expulsion the hoof of the fetus is forced through the roof of the vagina and into the rectum, producing a fistula" (Aanes, 1964).

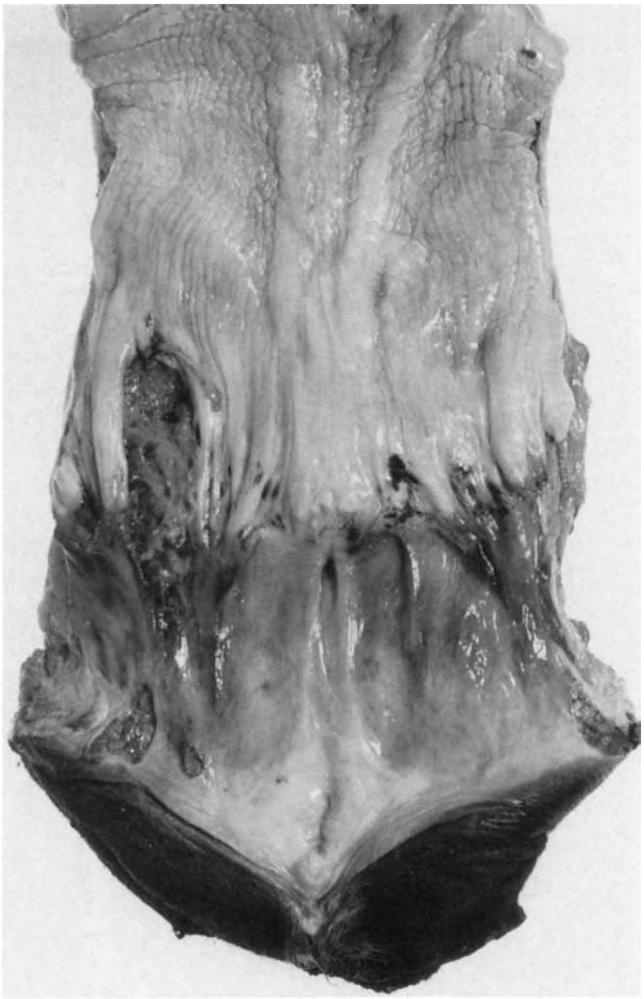

Fig. 12.11. Laceration of the caudal vagina and vestibule of a heifer. Acc. No. 9395.

Injuries Induced by Other Animals (Traumatic Anovulvitis)

When horned cattle run together, especially in confined areas, it is not unusual for lacerations of the vulva to occur. Deep injuries result in severe scarring and distortion of the vulvar labia.

Bite injuries of the bovine vulva are inflicted by pigs and dogs. The wounds become contaminated by bacteria and diphtheritic vulvovaginitis develops.

Eversion (Prolapse) of Transverse Cervical Folds

Enlargement and eversion of the transverse cervical folds adjacent to the vagina in cattle are secondary to traumatic parturient injuries. Considerable hemorrhage occurs in the connective tissue of the folds during a heifer's first parturition. During resolution of the hemorrhagic lesion, fibrous tissue proliferates and the folds increase in size. I have seen transverse folds protrude into the vagina by 30 days following parturition in first calf heifers. Repeated parturitions result in progressive enlargement and eversion of the cervical folds (Fig. 12.12).

Vaginal 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 caudal. Not infrequently, the entire vagina and cervix are prolapsed through the vulva. Vaginocervical prolapse is seen in all species of domestic animals but most commonly in the cow, especially Herefords, and the ewe" (Roberts, 1971).

Vaginal prolapse in ruminants usually occurs during advanced pregnancy and occasionally after parturition. Farquharson (1952) reported that "The support and fixation of the genital organs in the domesticated ruminant permits greater displacement and retroflexion than in most quadrupeds. The broad ligaments, being subiliac in their parietal attachment instead of sublumbar, have little to do with the support of the pregnant uterus. . . . In the normal and nonpregnant animal, this loose, inadequate sup-

Fig. 12.12. Prolapse of cervical folds of a cow. Acc. No. 2470.

port and fixation makes it possible in examination . . . to bring the cervix backward with a moderate degree of traction within sight of the lips of the vulva."

According to Arthur (1975), "an excessive deposition of fat in the perivaginal connective tissue and ligamentous relaxation may increase mobility of the vagina. Both these effects might be due to a state of endocrine imbalance, in which oestrogenic hormones predominate. The administration of stilboestrol is known to soften the genital ligaments and to increase the bulk of the genital tract."

Edgar (1952) stated that "In New Zealand in 1935, when the condition was more prevalent than usual, a survey conducted on 19 farms revealed an incidence varying from 1 to 8%." Vaginal prolapse occurred mostly in pregnant ewes in good condition, "more often in second and later pregnancies and usually within a fortnight before lambing." He reported that 50 (43%) of 115 affected ewes died. It also occurs in nonpregnant ewes that graze on subterranean clover (Bennetts *et al.*, 1946).

Gilts and heifers develop edema of the vulva, relaxation of the pelvic ligaments, tenesmus, and vaginal prolapse following ingestion of moldy corn and barley containing zearalenone.

In dogs, edema and eversion of a portion of the vagina occur, especially in Boxers, during proestrus and estrus.

Metaplasia

Squamous Metaplasia

The ducts of the vestibular glands of newborn calves, and probably of other species of domestic mammals, are lined by stratified squamous epithelium, reflecting estrogen stimulation. Squamous metaplasia of the cervical epithelium, mesonephric ducts, and the ducts of the major vestibular glands occurs in cows with persistent follicular cysts, in ewes on subterranean clover pasture, and in cattle and sheep with highly chlorinated naphthalene poisoning (McEntee and Olafson, 1953). I have seen marked keratinizing squamous metaplasia and cystic distention of the mesonephric ducts in the vagina (Fig. 12.13) of a bitch treated for a prolonged period of time with estrogen.

Fig. 12.13. Cystic mesonephric duct in the vagina of a bitch. Acc. No. 17885.

Glandular Metaplasia

Glands are not present in the normal ovine cervix but develop in ewes that have grazed estrogenic subterranean clover pastures for several years (Adams, 1976a; Lightfoot and Adams, 1979). The glands develop from the epithelium in the cervical crypts and become permanently cystic.

Dellmann and Carithers (1968) reported the presence of glands in the cervix of the goat, but Joshi *et al.* (1976) and Heydon and Adams (1979) did not find them in the goats that they examined. The latter authors suggested that cervical glands may develop in goats, as in sheep, as a consequence of estrogen stimulation. The goats that they examined came from semidesert country in which estrogen-containing clover did not grow.

Hyperplasia

Cystic hyperplasia of the cervical mucosa occurs in the bitch with cystic hyperplasia–pyometra complex as a result of chronic progesterone stimulation. The hyperplasia occurs in dogs treated with medroxyprogesterone acetate and persists following withdrawal of therapy, even though the uterine lesions regress.

Cystadenomatous polyps of the cervical mucosa occur in the bitch and may be confused with epithelial neoplasms. The polyps protrude through the external cervical os into the cranial vagina.

Riera *et al.* (1989) recorded a case of prolapse of cervical tissue in a 5-year-old maiden mare. The tissue could not be replaced; thus the mare was killed. The tissue arose from the right lateral wall of the cervix. It consisted of multiple folds and weighed 745 g. A smaller (88 g) mass with a wide stalk was attached to the dorsal rim of the urethral orifice.

The largest mass was covered predominantly by cervical epithelium. Some sections contained a few endometrial glands, indicating that the tissue arose from the junction of the cervix and uterus. The rest of the large mass consisted of areolar connective tissue. The smaller mass apparently arose from vaginal epithelium. Both lesions appeared to be benign. Although it was not mentioned in the article, the cervical lesion may have been a congenital malformation that enlarged due to edema.

Neoplasia

The WHO classification of tumors of the female genital tract is followed for discussion of the neoplasms of the cervix, vagina, and vulva (McEntee and Nielsen, 1974).

Tumors of the Cervix

Epithelial Tumors. Primary carcinomas of the cervix and breast are the most common malignant neoplasms in women of reproductive age (Abel, 1973). In contrast, epithelial neoplasms of the cervix are very rare in all species of domestic mammals.

Monlux *et al.* (1956a) reported one adenocarcinoma and one squamous cell carcinoma of the bovine cervix. Metastatic lesions were present in the lungs and in various lymph nodes in both animals. Anderson and Sandison (1969) reported three squamous cell carcinomas of the bovine cervix. The affected cows ranged in age from 6 to 8 years. Metastases were present in the liver, lungs, and peritoneum and in the iliac, sublumbar, hepatic, mediastinal, and bronchial lymph nodes.

Udall *et al.* (1926) reported a cervical carcinoma from a 6-year-old, debilitated Holstein cow. Metastases were present in the uterus, broad ligaments, mediastinal lymph nodes, and lungs. The specimen was available for examination half a century later because it had been kept in the museum at the New York State Veterinary College. The thick-walled cervix was 10.5 cm long and 10 cm wide (Fig. 12.14). The cervical mucosa was ulcerated and covered by a thick layer of necrotic tissue. Exudate was present in the uterine lumen. The neoplasm consisted of narrow cords and small nests of anaplastic squamous cells in a moderate amount of dense connective tissue stroma. The amount of stroma was much less than that in adenocarcinomas of the bovine uterus. Necrosis of neoplastic cells in the center of some of the cords and nests resulted in the formation of pseudoglandular structures. The growth extended through the entire wall of the cervix and tumor thrombi were present in numerous lymphatics. The stroma was diffusely infiltrated by plasma cells and lymphocytes, especially in the tumor adjacent to the superficial necrotic tissue. The neoplasm was diagnosed as an anaplastic squamous cell carcinoma. It is the only bovine cervical carcinoma that I have had the opportunity to examine.

Dämmrich and Lettow (1968) reported the clinical signs in a 14-year-old Dachshund bitch with an ade-

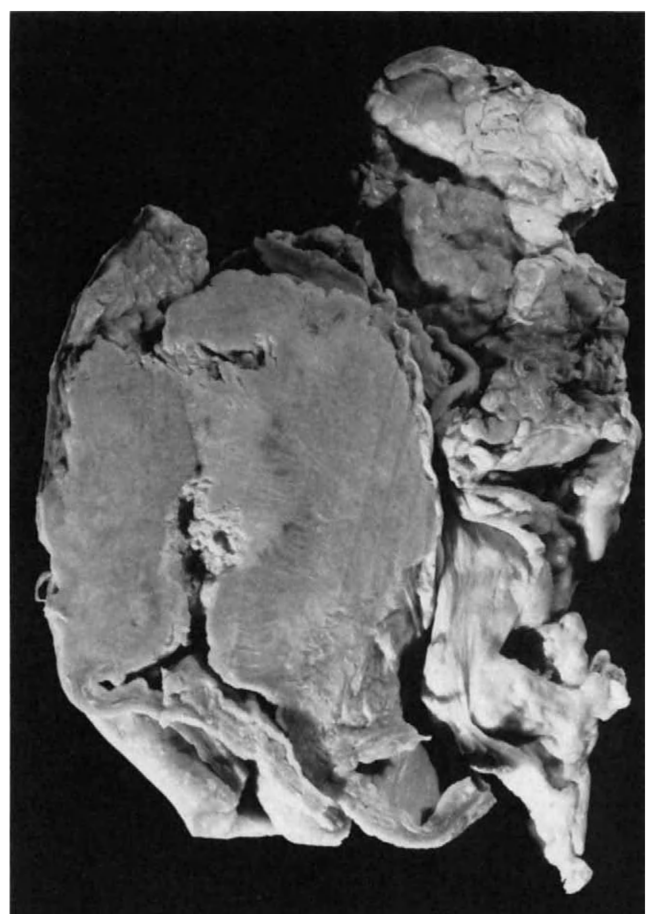

Fig. 12.14. Carcinoma of the bovine cervix. Acc. No. 16363.

nocarcinoma of the cervix and described the gross and microscopic features of the neoplasm.

Mesenchymal Tumors. The leiomyoma is the most common neoplasm affecting the cervix of domestic mammals. The fibroma occurs much less frequently. The malignant counterparts of these neoplasms occur occasionally. It is not unusual for multiple leiomyomas to occur in the uterus, cervix, and vagina of the bitch. The histologic features of the neoplasms are similar in all locations in the reproductive tract.

Tumors of the Vagina and Vulva

Epithelial Tumors

Papilloma. This is a benign, papillary, epithelial tumor with scant to moderate fibrous tissue stroma. Cutaneous papillomas occur in all species of domestic mammals and occasionally in the vulvar skin. They usually occur in relatively young animals, are due to the papilloma virus, and regress following the development of immunity.

Parish (1961) reported the transmission of papillomas of the preputial diverticulum in swine to the genital tracts of male and female pigs. Inoculation of the vulvar or preputial skin with cell-free filtrates of the papilloma resulted in the development of macroscopic lesions within 4 to 10 weeks. The early lesion consisted of thickening of the basal (Malpighian) layer and marked prolongation of the rete ridges. Mitotic figures were frequent in the basal cells in the epidermis. The lesion progressed to a papillomatous structure with parakeratosis. The dermis was hyperemic and infiltrated by lymphocytes, plasma cells, and mast cells. Cytoplasmic inclusions were found in the papillomas but it was concluded that they were "a product of cellular degeneration rather than the specific sequel to the presence of the virus" (Parish, 1961). The lesions regressed spontaneously and the animals had solid immunity to reinfection.

Squamous Cell Carcinoma. Squamous cell carcinoma of the vulva occurs predominantly in cattle, sheep, and goats and occasionally in other species of domestic mammals. The neoplasm occurs most frequently in countries with high levels of solar irradiation. It occurs in areas of the skin with a lack of melanin pigment and a deficient covering of wool or hair. Photosensitization predisposes animals to the development of the lesion. It is suspected that the papilloma virus may have some role in the production of the carcinoma (Vanselow and Spradbrow, 1983).

The incidence of squamous cell carcinomas of the vulva of ewes increased in Australia and South Africa following the use of a radical, surgical procedure for removal of perineal skin folds to reduce the incidence of cutaneous myiasis. The operation, combined with short tail docking, exposes the vulva and surrounding perineal skin to ultraviolet radiation and squamous cell carcinomas develop. Hawkins *et al.* (1981) conducted a survey of the incidence of squamous cell carcinomas of the perineal region in Western Australian sheep. Data were collected from 80 farms and the mean prevalence in ewes of all ages was 2.29% (range 0.12 to 4.0%). "The prevalence increased with age, from 0.05% in 1- to 2-year-old ewes to 3.09% in ewes over 5 years of age" (Hawkins *et al.*, 1981). The vulva was involved in 88.9% of the cases, the tail in 23.8%, and the perineum in 12.8%.

The lesion appears to originate from the ventral labial commissure and spreads dorsally along the mucocutaneous junction on both sides of the vulva (Vandegraaff, 1976). The surface of the carcinoma becomes ulcerated, necrotic, and covered by exudate and blood. The neoplasm is slow to metastasize.

Burdin (1964) reported that squamous cell carcinoma of the vulva of Ayrshire cattle in Kenya occurred only in unpigmented areas of the vulva. Lesions were not found in Sahiwal cattle, which have pigmented vulvar skin. The vulvar lesions progressed from acanthosis to papilloma to squamous cell carcinoma. The acanthotic lesions consisted of "discrete translucent white thickenings of the skin, smooth and very slightly raised above the general surface, with rounded edges; they tended to become confluent and to cover in irregular fashion virtually the whole of the unpigmented part of the vulva" (Burdin, 1964). There was a transition from this early lesion to papilloma to carcinoma. The papillomas were discrete raised nodules with an irregular surface. The carcinomas were deep seated, ulcerated, and infected masses of tissue. "In advanced cases, the whole vulva was obliterated." Four affected animals were killed and metastatic lesions were found only in the right external iliac lymph node of one cow that had advanced vulvar lesions. As in the ewe, the vulvar squamous cell carcinoma of the cow is slow to metastasize.

Carcinoma of the Canine Vestibule. I have examined biopsy specimens from six neoplasms located in the canine vestibule. One dog was a Scottish Terrier and the rest were mixed breeds. They ranged in age from 8 to 15 years. The specimens were submitted to the New York State Veterinary College Diagnostic Laboratory, with very little information provided concerning clinical signs, gross features of the neoplasms, and their exact location. Follow-up information was provided on only one case. The locations of the neoplasms in three bitches were: lateral wall of the vestibule, floor of the vestibule near the clitoris, and floor of the vestibule near the urethral orifice. Neoplastic glands (Fig. 12.15) were present in the periphery of some of the tumors and the central portions consisted of solid masses of bizarre epithelial cells with abundant eosinophilic cytoplasm. Signet ring cells with a single, large, mucus-containing vacuole were a prominent feature of all the specimens. The size of the cells was quite variable and many contained two or more nuclei. Two to five mitotic figures were present in high-power fields. The lymphatic vessels were packed with solid sheets of neoplastic cells. The only dog that I was able to follow after surgical removal of a vestibular neoplasm was killed about 3 months later because of debility. The owner did not permit a postmortem examination.

The site of origin of these carcinomas was not determined. The primary site may have been in the vestibular glands, urinary bladder, or urethra. The neoplasm that was located on the floor of the vestibule near the urethra probably originated in the urinary tract.

Carcinoma of the Urinary Tract. Magne *et al.* (1985) reported urinary tract carcinomas that involved either the vagina or vestibule or both of seven ovariectomized bitches that were 10 to 12 years old. "The most consistent clinical signs were hematuria, hematocolpos, stranguria and pollakiuria." The neoplasms extended from the bladder or urethra to the urethral papillae and then to the vagina or vestibule. "Four bitches had transitional cell carcinomas of the bladder. Three bitches had a primary squamous cell carcinoma of the urethra. The tumors invaded and separated urethral and vaginal or vestibular smooth muscle" (Magne *et al.*, 1985). There was a limited description of the histology of the neoplasms but they were well illustrated by photomicrographs.

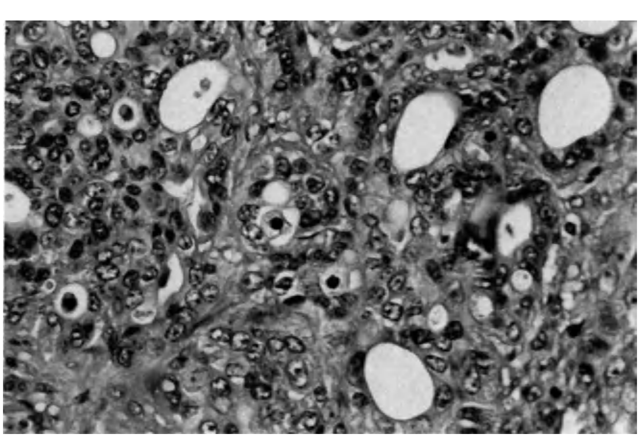

Fig. 12.15. Carcinoma of the vestibule of a 13-year-old dog. Acc. No. 16601.

Metastatic Carcinoma of the Mammary Gland. Roszel (1974) reported the presence of metastatic neoplastic cells in vaginal smears from five bitches with carcinomas of the caudal mammary glands. Four of the animals were submitted for necropsy. Gross lesions were not evident in the reproductive tract but mammary carcinoma cells were found in the lymphatic vessels of the vestibule in three animals. One bitch also had metastatic lesions in the vessels between the muscle and serosa of the urethra, urinary bladder, and vagina. Tumors were present in the inguinal lymph nodes of all dogs.

Mesenchymal Tumors

Fibropapilloma (Fibroma). The fibropapilloma is a transmissible tumor of the vulva and vagina of heifers and the penis of young bulls (McEntee, 1950). It is due to a papilloma virus and may be present in several animals that run together. The lesions appear grossly as firm, elevated, white or pink masses of tissue with a smooth or cauliflower-like surface. They are usually located in the mucosa of the vestibule but can occur in the vulvar skin or in the vagina. The lesion may be single or multiple.

The fibropapilloma consists predominantly of proliferating fibrous tissue with an epithelial covering of varied thickness. The early rapidly growing lesion consists of fibroblasts, little collagen, and fairly numerous mitotic figures. The tumor cells are arranged in characteristic interwoven bundles. Lesions at this stage of development have been reported incorrectly as fibrosarcomas. The amount of collagen increases concurrently with the development of immunity.

Leiomyoma and Leiomyosarcoma. The leiomyoma is a common neoplasm of the vagina and vestibule of the bitch (Fig. 12.16) and occurs occasionally in these locations in other species of domestic mammals. Brodey and Roszel (1967) reported a total of 96 neoplasms of the uterus, vagina, and vulva in 90 bitches from 3073 tumor-bearing animals out of a total population of 75,000 dogs. Eighty-five tumors were from the vulva and vagina and 11 from the uterus. Sixty-six leiomyomas were present in the vulva and vagina and 10 in the uterus. Most of the leiomyomas arose from the vestibule. The incidence of leiomyomas was significantly higher (at the 5% level) in Boxers. Leiomyosarcomas were found in the vestibule or vagina of three animals. The other neoplasms of the vulva and vagina included nine transmissible venereal tumors, five lipomas, one mast cell tumor, and one epidermoid carcinoma.

Fibroma and Fibrosarcoma. Fibrous tumors of the reproductive tract occur much less frequently in do-

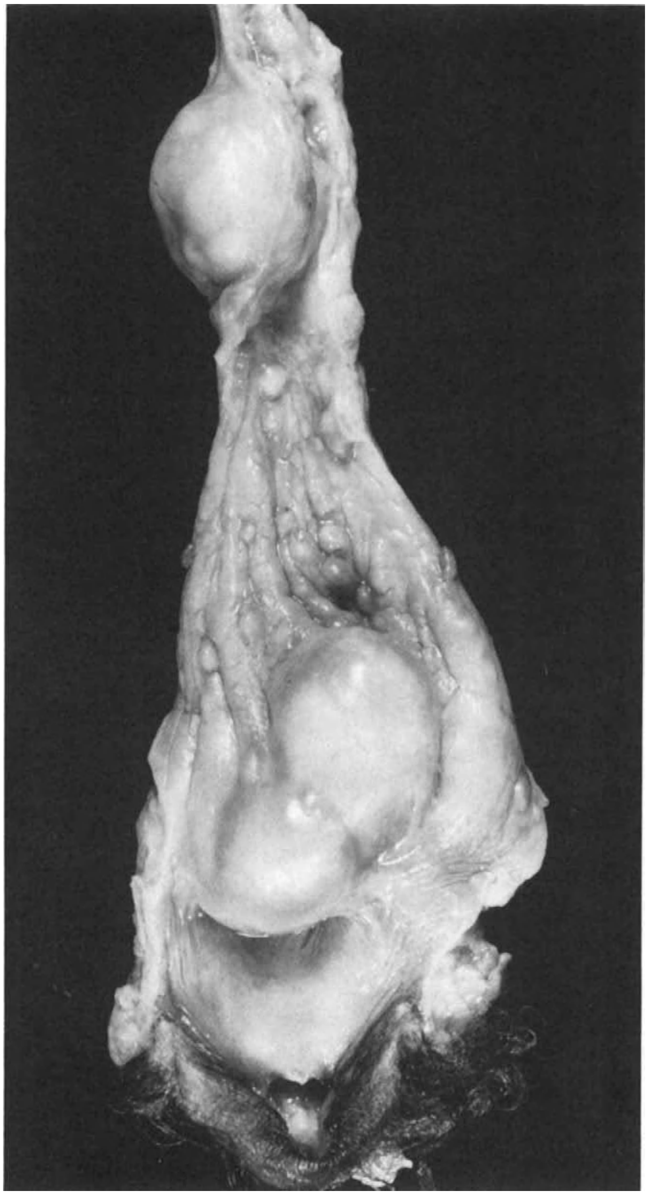

Fig. 12.16. Multiple leiomyomas in canine vagina. The tumors have a broad base. Acc. No. 17563.

Fig. 12.17. Fibromatous polyps in canine vagina. The large caudal polyp had protruded through the vulva. Acc. No. 17564.

mestic mammals than smooth muscle neoplasms. Brodey and Roszel (1967) did not report any in their survey. It is probable that many of the reported fibromas of the vagina of dogs are fibromatous polyps (Fig. 12.17) resulting from proestrual and estrual edema. Furthermore, many leiomyomas undergo fibrous dysplasia.

Lipoma. Lipomas of the vulva and vagina occur predominantly in the bitch.

Transmissible Venereal Tumor (Sticker's Tumor, Venereal Granuloma, Infectious Sarcoma, Transmissible Lymphosarcoma, Histiocytoma). The transmissible venereal tumor is a canine neoplasm that is usually transmitted during coitus. It is the first tumor to have been transplanted experimentally from one animal to another (Novinsky, 1876). The external genitalia of both sexes are affected and it occurs occasionally in other areas of the skin. It usually regresses spontaneously but can occasionally behave as a malignant neoplasm and metastasize to internal organs. Single or multiple tumors may be present in the vestibule and vagina. According to Bloom (1954), the most common site is the ventral portion of the caudal vaginal wall. He stated that "The tumor is relatively firm, nodular or papillary, often with a broad base and the surface is either smooth, rough, or ulcerated." Large neoplasms may occlude the vaginal lumen and protrude from the vulva.

The tumor cells are arranged in densely packed masses separated by fine strands of connective tissue containing collagen and reticulum fibers. The cells are round to polyhedral, rather uniform in size, and have abundant clear or pale eosinophilic finely granular cytoplasm. Formalin fixation frequently causes shrinkage of the cytoplasm so that the cell outlines are not evident. The nuclei are large, round to oval, and relatively vesicular, and usually contain a single prominent nucleolus. Mitotic figures are usually numerous, with two to eight per high-power field, but the frequency varies depending on the stage of growth of the neoplasm. Lymphocytes, macrophages, eosinophils, and tissue mast cells are scattered through the tumor. Neutrophils are often present in animals showing regressive changes, including marked vacuolization of the cytoplasm of the tumor cells. The histogenic origin and the etiology of the tumor are unknown.

The karyotype of the normal dog is 76 XY and all the autosomes are acrocentric. On the other hand, the cells of the transmissible venereal tumor usually contain 59 chromosomes of which 42 are acrocentric and 17 are metacentric (Makino, 1963).

Embryonal Sarcoma of the Porcine Vagina. Monlux *et al.* (1956b) and Monlux and Monlux (1972) reported the occurrence of embryonal sarcoma in the vagina of pigs 6 months to 1 year of age. They stated that "these tumors bear some resemblance to the 'grape-like' or 'botryoid' sarcomas of the vagina of children and young adults." The vagina, cervix, and uterine body "merged into a continuous single, enlarged, hyperplastic structure measuring about 45 cm in length and 15 cm around the greatest circumference of the vagina." The vaginal mucosa was arranged into 2- to 3-cm-thick rounded or annular folds. The submucosa and muscularis were thick, firm, and gray or soft and mucoid. The uterine horns and ovaries were normal. The thickening of the vagina, cervix, and uterine body was due to "a proliferation of mesenchymal cells in an edematous, vascular, and fibrous connective tissue stroma." The overlying epithelium was intact. The internal iliac, sublumbar,

Fig. 12.18. Single lymphosarcoma in bovine vagina. Acc. No. 783.

Fig. 12.19. Numerous small lymphosarcomas in bovine vagina. The gross appearance was that of vaginitis. Acc. No. 8442.

and rectal lymph nodes were hyperplastic but no metastases were found.

Lymphosarcoma. Lymphosarcomas occur in the vagina of cows as single (Fig. 12.18) or multiple lesions (Fig. 12.19). Usually, the vestibule and cervix are not involved.

Miscellaneous Neoplasms of the Vulva. Dermal and epidermal neoplasms that are usually found on other parts of the body occasionally develop in the labial skin (Weiss and Frese, 1974). The vulva, anus, and surrounding perineal skin are common sites for the development of melanomas in gray horses (Levene, 1971). Gleicher *et al.* (1979) reported that "the vulva, as the main site of occurrence, represents up to nine percent of all cutaneous melanomas (CMM), although it represents only one percent of the human skin area. Malignant melanoma is the second most common cancer of the vulva and the gynecologist will see more cases of MM than would be expected in an area of skin the size of the vulva."

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Chapter 13

Scrotum and Testis: Anatomy and Congenital Anomalies

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- Appendix Testis
- Appendix Epididymis
- Testes of Various Species of Domestic Mammals

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Bibliography

Anatomic Features

Scrotum

The testes enter the scrotum midway through fetal life in ruminants and shortly before birth in horses. Baumans *et al.* (1981) stated that the testes of the dog "pass into the inguinal canal on the third or fourth day of postpartum age and are located in the scrotum on the 35th postpartum day." Horses, pigs, dogs, and cats have pouched scrota; bulls, rams, and buck goats have pendulous scrotal sacs. The scrotal skin is thin and has very little subcutaneous fat except in obese animals. The skin is sparsely covered by hair in bulls, horses, and dogs but is well covered by wool in several breeds of sheep. Numerous large sweat glands are present in the scrotal skin of sheep and cattle. The skin is often darkly pigmented in all species of domestic mammals. The tunica dartos muscles are thickest under the distal part of the scrotum, and thus their contraction results in elevation of the testes.

Testes

Testes, rather than *testicles,* is the correct term for the primary male reproductive organs. The literal meaning of testicle is a "small testis"; however, the term is used occasionally as a synonym for *testis.* The *sustentacular cells* (supporting cells, nurse cells) of the testis are usually referred to as "Sertoli cells," and the endocrine *interstitial cells* are often called "Leydig cells." It seems unusual that Sertoli's name is used more frequently than Leydig's for identifying specific cells of the testis. To encourage the proper usage of veterinary terms, *eponyms* are not used in this text except in citation of references. This is in contrast to the wide usage of eponyms in human medicine.

The term *germinal epithelium* is sometimes used incorrectly as a synonym for *seminiferous epithelium.* Waldeyer created the term "germinal epithelium" in 1871 for the coelomic epithelium covering the gonads of mammals. He originally thought that the surface epithelium gave rise to germinal cells, but he retracted this idea in 1906 (Roosen-Runge, 1977).

Mammals are the only animals in which the testes descend from the abdominal cavity into a scrotum. The degree of descent differs among the various species of domestic mammals. The testes are held close to the body in the boar and cat and descend into a well-developed pendulous scrotum in the bull, ram, and buck goat. The epididymides are located dorsally or caudomedially on the testes, depending on the degree of descent of the gonads into the scrotal pouch. The left testis can be differentiated from the right, in specimens that have been removed from the body, by holding the testes by their spermatic cords in their normal position. The epididymis will be approximately lateral, and the ductus deferens will be medial. The pole of the testis adjacent to the head of the epididymis is the head extremity (extremitas capitata), and the one near the tail of the epididymis is the caudal extremity (extremitas caudata). The edge of the testis adjacent to the epididymal attachment is the attached or epididymal border, and the opposite side is the free border. The testis is enclosed by peritoneum (tunica vaginalis), a network of small blood vessels and delicate areolar tissue (tunica vasculosa), and a thick layer of fibroblasts, bundles of collagenous fibers, smooth muscle cells, and nerve endings (tunica albuginea). Internally, the spaces between the seminiferous tubules contain blood vessels, lymph vessels, nerves, fibrocytes, and interstitial (Leydig) cells.

For examination of the testis, the spermatic cord and epididymis should be dissected from the gonad after the structures have been examined for gross lesions. The gonads are then weighed and measured. A midsagittal incision should be made through the testis so that the mediastinum testis is exposed. After the midsagittal cut is made and the surface is examined, each half should be cut transversely into slices approximately 5 mm to 1 cm wide (Fig. 13.1). Then each incised piece can be folded over and the cross sections examined. If this procedure is not used, many small lesions, including early tumor formation, may be overlooked. The cut surface of a normal testis bulges above the surface. If the testis does not bulge, it indicates that severe degeneration of the seminiferous tubules has occurred. The color of the testis varies among species and also according to age. The color depends on the amount of pigment present in the interstitial cells, and this pigment tends to increase with age. The normal color of the bovine testis is tan to tannish brown. The testes of mature stallions and boars are darker than those of bulls.

Fig. 13.1. Bovine testis cut midsagitally. One-half of the gonad was cut transversely into 1-cm segments. Acc. No. 18329.

For routine histologic examination of a testis, a section of tissue should be taken from three levels, including the head extremity, middle part, and caudal extremity. Testicular tissues should be handled gently and should be incised with a very sharp knife. Otherwise, severe compression artifacts will be produced. Quite frequently, there will be compression artifacts around the peripheral portion of a block of tissue so that in many cases the peripheral tissue should be ignored when examining histologic detail. A hard fixative, such as Bouin's solution, should be used for preserving testicular tissue. Formalin fixation is very poor for testicular tissue since it is a soft fixative. Histologic interpretation of formalin-fixed testis is usually difficult because the procedure of dehydration in graded alcohols creates severe shrinkage artifacts. Bouin's solution results in fewer artifacts.

A variety of special stains are useful for studying the normal histology and pathology of testicular tissue. Periodic acid–Schiff (PAS) is useful for studying stages of the spermatogenic cycle. Masson's trichrome stain is used for differentiating connective tissue from interstitial cells. An elastic tissue stain is useful for studying the basement membrane of the seminiferous tubules in cases of degeneration. The elastic tissue contracts in degenerate tubules and appears as a wavy band of tissue. A reticulum stain outlines the cytoplasm of the sustentacular cells and the cellular membrane of the interstitial cells. Frequently, a complete ring of black material will be deposited around each interstitial cell. Oil red O is useful for demonstrating lipid in the cytoplasm of interstitial cells and sustentacular cells.

Seminiferous Tubules. The seminiferous tubules are small convoluted tubules, both ends of which are connected through receptacles and tubuli recti to the rete testis. They are lined by seminiferous epithelium and surrounded by elastic tissue. The maturation of germinal cells in the seminiferous epithelium occurs in waves. Two principal methods have been developed for classification of the stages of the seminiferous epithelium. One is based on the development of the acrosome, and the other is based on germ cell association.

Classification Based on Acrosome Development. Classification based on acrosome development has been reported in the ram, bull, dog, cat, monkey, and man by Clermont and Leblond (1955). Pieces of testis, less than a cubic centimeter in size, were fixed in Zenker-formal, Orth, or Bouin's solution and stained by the periodic acid–Schiff technique. The tissues were counterstained by Harris' hematoxylin. Spermiogenesis was divided into four periods referred to as the Golgi, cap, acrosome, and maturation phases. The four phases were subdivided, based on changes in the acrosome and head cap, into stages referred to as "steps" of spermiogenesis. Clermont and Leblond (1955) reported that "At the Golgi phase PA–Schiff-reactive particles appear in the idiosome and fuse into the acrosome granule—a structure composed of an inner and an outer zone. At the cap phase the outer zone expands on the nuclear surface to become the head cap. . . . During the acrosome phase, as the acrosome granule enlarges to become the acrosome, the differences between inner and outer zones are no longer distinct, and therefore, the acrosome appears homogeneous. . . .During the last or maturation phase, the PA–Schiff staining of the acrosomic system decreases gradually."

Classification Based on Germ Cell Association. Roosen-Runge and Giesel (1950) and Ortavant *et al.* (1977) defined eight stages in the seminiferous epithelium as follows:

Stage 1. From the end of the release of spermatozoa from the seminiferous epithelium until the beginning of elongation of spermatid nuclei.

Stage 2. From the elongation of the spermatid nuclei until the onset of grouping of spermatids into bundles.

Stage 3. From the formation of spermatid bundles to the beginning of the first maturation division of spermatocytes.

Stage 4. From the appearance of the first maturation division to the end of the second maturation division.

Stage 5. From the end of the second maturation division until the appearance of dusty chromatin in young spermatid nuclei.

Stage 6. From the appearance of dusty chromatin in the nuclei of spermatids until the movement of spermatozoa bundles toward the lumen of the seminiferous tubles.

Stage 7. From the start to the end of the movement of spermatozoa bundles toward the lumen.

Stage 8. From the completion of the central movement of spermatozoa to their release into the lumen.

Receptacles. The receptacles (transitional zones) are the connecting pieces between the terminal parts of the seminiferous tubules and the tubuli recti. Marin-Padilla (1964) stated that "They are interpreted, together with the tubuli recti and the rete testis, as the true connecting structures between the testes and the mesonephric excretory system. They are only apparent, as connecting pieces, during sexual maturity when spermatozoa become ready for discharge." He reported that "The epithelium of the receptacle, the tubuli recti and the rete testis is identical except for the presence of ciliated cells in the rete testis, cells which are not present in the receptacles or the tubuli recti. The epithelial cells of the receptacle are histologically different from the Sertoli cells of the seminiferous tubles in their size, nucleus, and arrangements." He found receptacles in the testes of the horse, dog, and cat. They are also present in the testes of other species of domestic mammals. Receptacles are present in the mule but lack communication with the lumina of the seminiferous tubules.

Tubuli Recti. The tubuli recti (rete tubules, straight seminiferous tubules) connect the receptacles with the rete testis. In most species, they are located in the central portion of the testis adjacent to the mediastinum testis, which contains the rete testis. They are scattered throughout the equine testis and provide landmarks for histologically differentiating equine testes from those of other species of domestic mammals.

Mediastinum Testis. The mediastinum testis is a mass of fibrous tissue that is located in the central part of the testis and is continuous with the tunica albuginea. It contains the rete tubules.

Rete Testis. Dym (1976) stated that "The rete testis consists of a series of interconnected wide channels lined with a simple cuboidal to columnar epithelium, resting on a thick basal lamina. Beneath the basal lamina dense bundles of collagen fibrils and a few blood vessels, lymphatics, or nerve tissue are found." Amann *et al.* (1977) reported that "Although the mediastinum was not conspicuous in the equine testis, a rete testis consisting of anastomosing tubules surrounded the central vein. The rete testis extended about 2/3 of the length of the testis and penetrated the tunica albuginea before connecting with the efferent ducts." The rete testis is located in the central portion of the testis in most species of domestic mammals but is in a dorsally eccentric position in the stallion. "If any area within the testis containing rete testis tubules, loose connective tissue, and blood vessels is considered to constitute a mediastinum testis, the equine testis must be considered to have an atypical, relatively inconspicuous, but true mediastinum" (Amann *et al.*, 1977).

Appendix Testis

The appendix testis, the homologue of the infundibulum of the uterine tube, is always present in the stallion, occasionally in the boar, ram, goat, and dog, and never in the bull. The appendix testis is located on the surface of the testis adjacent to the head of the epididymis (Fig. 13.2). It may be flat, rounded, or lobular and is usually a few millimeters in diameter and length. Histologically, it consists of vascular connective tissue and smooth muscle with channels lined by cuboidal or columnar epithelium.

Appendix Epididymis

The appendix epididymis is considered to be of mesonephric duct origin. It is occasionally present in all species of domestic mammals as a cystic structure located between the head of the epididymis and the testis or on the surface of the testis adjacent to the epididymal head. The vestigial remnant is discussed in more detail in Chapter 16.

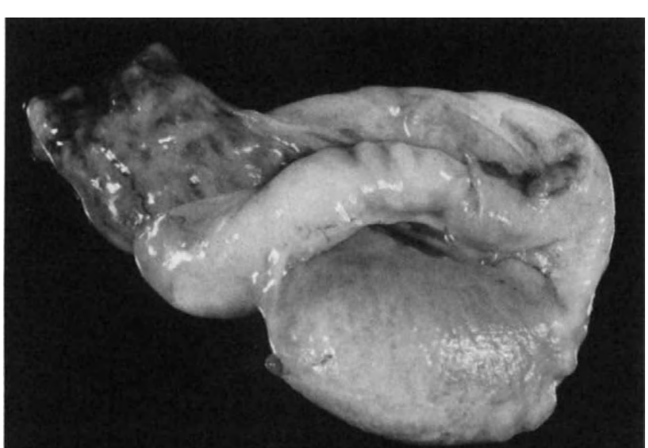

Fig. 13.2. Appendix testis of a 14-month-old stallion. It is a papillary structure on the testis below the head of the epididymis. Acc. No. 16448.

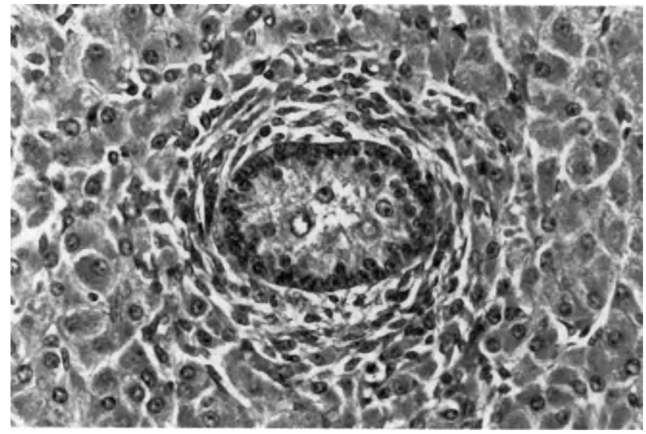

Fig. 13.3. Enlarged interstitial cells surrounding a seminiferous tubule in an equine fetus. ×222. Acc. No. 11176.

Testes of Various Species of Domestic Mammals

Stallion. Nishikawa (1959) reported that the fetal equine testes weigh approximately 35 g each at 220 days of gestation and 5 to 10 g at the end of gestation. The enlargement of the gonads in the equine fetus is due to hyperplasia and hypertrophy of the interstitial cells (Fig. 13.3), and the decrease in weight is due to degeneration of these cells (Fig. 13.4). Testicular weight remains relatively constant from the time of birth until about 10 months of age. Then the weight begins to increase rather slowly until the 17th or 18th month, when a more rapid development generally takes place. The testes remain small for a longer period of time when their descent is delayed. Nishikawa (1959) stated that "the left and right testes differ from each other in development. In general, the left testis begins developing first, and its development is

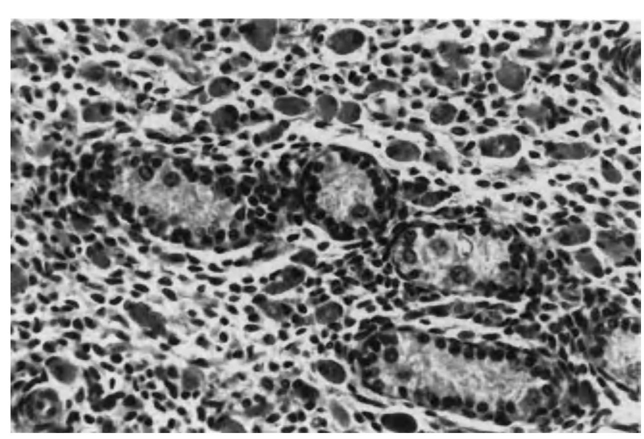

Fig. 13.4. Pigment-laden macrophages in interstitial tissue in the testis of a 30-day-old colt. ×222. Acc. No. 18773.

more rapid than that of the right testis. Thus, at the time of vigorous testis development, about 20 months after birth, there is a great difference in development between the left and right testis of one individual." Nishikawa found that the left testis was larger than the right in about 80% of 279 horses whose age varied from less than a month to 54 months.

The fetal testis is pale tan when it is enlarged but becomes dark brown when the interstitial cells degenerate in advanced pregnancy. The testis of the newborn colt is dark brown and remains dark until it begins to enlarge later in life. The color begins to fade as the testis enlarges. The process of fading occurs more rapidly on the side of the testis adjacent to the epididymis. The pale color is due to the disappearance of pigment-laden macrophages in the interstitium and the formation of lumina in the seminiferous tubules (Fig. 13.5). Nishikawa (1959) stated that "In testes of 30 to 40 g, there still remains the dark portion 0.2 to 0.3 cm in width along the circumference. With a further increase in testis weight, the dark brown portion becomes smaller, and in testes of 70 g there are still some brown spot or strings on the circumference." The brown color disappears in testes larger than 100 g.

Johnson and Neaves (1981) reported that "Age-related changes in the Leydig cell population of horses between 2 and 20 years old were characterized by a twofold increase in Leydig cell number per gram parenchyma, a threefold increase in Leydig cell number per testis, a threefold increase in Leydig cell volume per gram parenchyma, and a fivefold increase in Leydig cell volume per testis. Due to the increased volume of Leydig cells per gram of testicular parenchyma and the increased size and accumulation of lipofuscin granules in individual cells, the gross appearance of the parenchyma becomes darker with age." They stated that the average weight of a testis was 117 g at 2 to 3 years of age, 161 g at 4 to 5 years, and 213 g at 13 to 20 years.

The seminiferous tubules are connected to the rete tubules by short, straight passages known as tubuli recti. Some use the term "straight seminiferous tubules" for these structures, but the term is not appropriate because they do not produce sperm. Tubuli recti are located adjacent to the centrally placed rete testis in most species of domestic mammals but are scattered throughout the equine testis (Fig. 13.6).

The mediastinum testis is visible in young colts as a pale, narrow band of tissue extending about two-thirds of the distance from the head of the testis into the center of the gonad. The connective tissue surrounding the rete testis decreases as the testis grows, so that in adult horses the mediastinum testis is often overlooked on gross examination because there is much less connective tissue surrounding the rete tubules than is present in other species of domestic mammals.

Bull. Bovine testes are elongated, oval, and situated in a pendulous scrotum with the long axis placed dorsoventrally. The individual testicular weight of the dairy bull is about 230 to 250 g at 1 to 2 years of age, 300 g at 4 to 5 years, and 365 g at 6 years and older. The testes of some normal bulls weigh as much as 550 g each. Bulls do not have an appendix testis, but an appendix epididymis is present occasionally. The cut section of a normal bovine testis bulges considerably above the incised surface. A prominent mediastinum testis, containing rete tubules (Fig. 13.7), extends about four-fifths of the distance down through the center of the gonad. Interstitial cells are more numerous in Guernsey and Jersey bulls than in other dairy breeds.

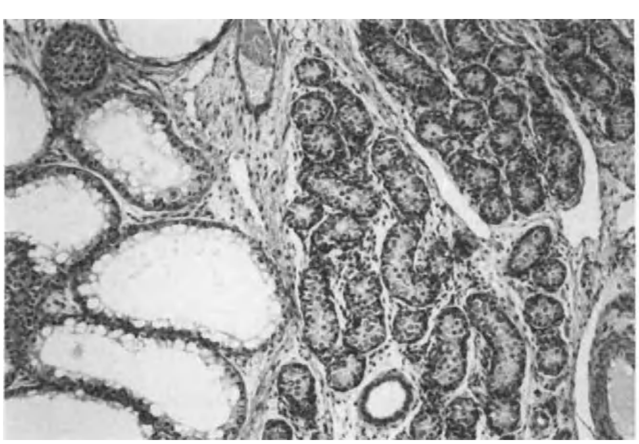

Fig. 13.5. Testis from a yearling colt with uneven development of the seminiferous tubules. ×89. Acc. No. 6057.

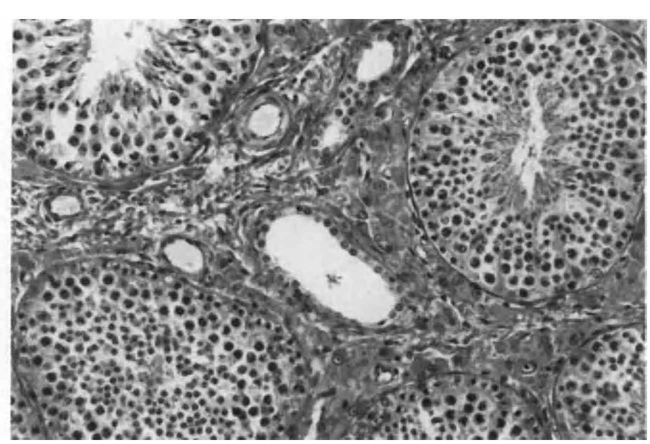

Fig. 13.6. Tubulus rectus between seminiferous tubules of an equine testis. ×178. Acc. No. 18640.

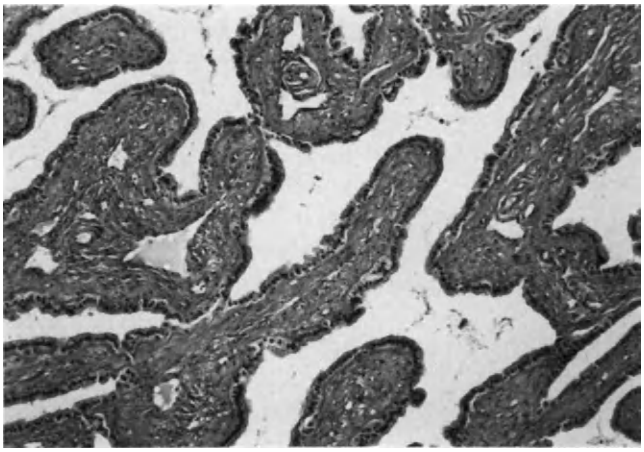

Fig. 13.7. Bovine rete testis with anastomosing tubules lined by cuboidal epithelium. ×89. Acc. No. 14072.

Lennox and Logue (1979) examined the testes from 27 bulls, predominantly Ayrshires, at the time of slaughter. They estimated that "The average bull testis contain about 5.2 km of tubules." No significant difference was found between the left and right testis.

Goyal (1982) reported the results of light microscopic and ultrastructural studies of epithelial phagocytosis of sperm in the rete testis and ductuli efferentes in the bull. "Phagocytosed sperm in various stages of degeneration were found in the epithelial cells lining the rete testis and in the nonciliated cells of the ductuli efferentes. Phagocytosis was more prevalent in the rete testis than in the ductuli efferentes. Besides the epithelial cells, degenerating sperm components and residual bodies were in the luminal macrophages of the rete testis" (Goyal, 1982).

Ram and Buck Goat. Testes of the ram and buck goat are relatively large and are located in a pendulous scrotum. The scrotal skin of the ram is well covered by hair. An appendix testis and appendix epididymis are occasionally present on the testes of both species. The testes of the ram weigh 200 to 300 g each, and those of the goat weigh 140 to 150 g.

Boar. The testes of the boar are located close to the body in a subanal position. The tail of the epididymis points caudodorsally and lies close to the anus. The average weight of each testis in mature animals is about 400 g, but each may weigh as much as 800 g in old boars. According to Bascom and Osterud (1925), the length of seminiferous tubules in the average boar is 6000 m. They estimated the length of the tubules of other species as follows: dog, 150 m; ram, 4000 m; and bull, 5000 m. Appendix testis and/or appendix epididymis are present occasionally. Testicular lymph nodes are frequently present along the dorsal part of the spermatic cord. There is considerable variation in their number, size, and location (Saar and Getty, 1975).

Dog. The canine testis is oval and is situated obliquely with the long axis running dorsocaudally. The epididymis is attached to the dorsolateral surface. The cut section of the testis does not bulge above the surface as much as that of ruminants or the boar.

During the study of 198 Beagle dogs between the ages of 37 weeks and 7.75 years, James and Heywood (1979) found that the weight of the testes increased markedly with advancing age. They reported that "The percentage of dogs with testes both weighing less than 10 g was highest (4.8%) for dogs with a mean age of 37 weeks. Over 50% of dogs attaining a mean age of 7.75 years had testes both weighing more than 30 g. The majority of dogs aged 46–125 weeks at the time of examination had a total testicular weight of 10–30 g."

Cat. The testes are located in an integumental scrotum that is covered by hair. The scrotum is located ventral to the anus.

Scott and Scott (1957) reported that the testes of kittens are fully descended at birth. They found that the combined weight of the testes increased from 20 mg at birth to 100 mg at weaning. Spermatozoa were present when the testes exceeded 1 g. The maximum weight of the testes was about 4 g.

Congenital Anomalies

Vascular Malformation of the Spermatic Cord

Osborne and Richardson (1965–1966) reported a greatly enlarged left testis in a newborn, purebred North Devon calf. Both testes were removed surgically when the calf was 2 weeks old. The left testis measured 20 × 14 × 12 cm. The surface vessels were enlarged and congested. The cut section revealed the presence of a hematoma, red to pink tissue, and areas of yellow necrotic-appearing material. The right testis was small and appeared congested.

Histological examination of the left testis revealed "the presence of the heamatoma, areas of necrosis, areas of oedema, and granulation tissue production with particular oedematous involvement of the artery walls. . . . There was very little evidence of normal testicular structure, no tubules being apparent" (Osborne and Richardson, 1965–1966). The right testis was apparently normal.

The authors considered the possibility that the testicular enlargement was due to a capillary hemangioma but concluded that "it may have been a haematoma resulting from partial obstruction of the vascular return from the organ by, for example, partial twisting of the spermatic cord." It would seem that a more likely cause of the lesion would be malformation of the pampiniform plexus of the spermatic cord allowing blood to be pumped into the testis and interfering with its return. It was not mentioned whether the spermatic cord was sectioned and examined.

Monorchia and Anorchia

Congenital absence of one of the testis (monorchia) or both testes (anorchia) is extremely rare in domestic mammals. The epididymis, as well as the testis, is usually missing. The defects have been reported in the dog and the stallion (Jamkhedhar and Ajinkya, 1966; Hobday, 1900a,b; Johnson *et al.*, 1976).

The report by Santschi *et al.* (1989) of monorchidism in three colts is questionable. The gross photo of the surgically removed tissue from the inguinal region of a yearling colt illustrates that the deferent duct and cremaster muscle end blindly rather than being attached to other tissue as occurs in cases of monorchidism.

I have seen only one case of monorchia in domestic mammals, and that occurred in a cat. The epididymis was present in the abdominal cavity on the side of the missing testis (Fig. 13.8).

Polyorchism (Polyorchidism, Testicular Duplication, Supernumerary Testes)

Duplication of the testes is rare in otherwise normal domestic mammals. According to Schlegel (1924), Cox and Nielsen each found three testes in stallions and Oliver found four testes in a mule. Foster (1952) reported the presence of three testes in a Thoroughbred colt. Earnshaw (1959) reported a similar case in a yearling colt.

Testicular Heterotopia

Testicular heterotopia is a condition in which nodules of testicular tissue are present on the peritoneal surface of the abdominal cavity. Todd *et al.* (1968) reviewed the literature on multiple heterotopic testicular tissue in pigs and reported seven additional porcine cases. Malignant neoplasia was often suspected on gross examination because of the presence of numerous 0.5- to 5-cm nodules of pinkish tan encapsulated tissue on many of the abdominal organs. Histologically, the tissue consisted of seminiferous tubules lined by sustentacular cells and a few spermatogonia. The interstitial cells were more numerous than normal. Epididymal tissue was not present. Heterotopic testicular tissue has not been reported in other species of domestic mammals.

Fig. 13.8. Epididymis from cat with aplasia of testis. ×2. Acc. No. 19228.

Synorchia (Testicular Fusion)

Fusion of abdominal testes is extremely rare in otherwise normal animals.

Splenic-Testicular Fusion

Noakes and White (1976) reported a case of fusion of the left testis and spleen in a 5-year-old pony. It was purchased as a gelding, but it showed intense masculine behavior. A single scar was present in the scrotum, and testes could not be palpated in the scrotum or in the external inguinal ring. Exploratory surgery of the left inguinal region "revealed a small, poorly developed vaginal sac in which the tail of the epididymis was identified. Traction and gentle dilation of the inguinal ring did not induce descent of the testicle. The abdomen was explored through a left paramedian incision. The left testicle was readily identified in the anterior pelvic cavity, but it was difficult to exteriorize the organ through the incision" (Noakes and White, 1976). The testis was separated from the spleen by blunt dissection; the spermatic cord was ligated and the testis removed. "When the pony was re-examined three months after the operation, its masculine behavior had disappeared."

Putschar and Manion (1956) reviewed the literature concerning 26 cases of splenic-gonadal fusion in man and recorded four additional cases. They stated that the anomaly occurs in two forms: "1. Continuous splenic-gonadal fusion in which a continuous cord-like structure connects the spleen and the gonadal-mesonephric structures; 2. Discontinuous splenic-gonadal fusion in which the fused spleno-gonada-mesonephric structures have lost continuity with the main spleen and appear as a special variant of accessory spleen. . . . The splenic-gonadal fusions, as would be expected, involved the left gonad in all cases with the possible exception . . ." of one case in which it was not stated which gonad was affected. The majority of the cases occurred in the male with a male/female ratio of nine to one. In some cases, the affected testis had descended into the scrotum when the gonad was attached to an accessory spleen.

Splenic-Testicular Fusion and Arrested Testicular Development

Frandson *et al.* (1960) reported an unusual case of arrested testicular development in a light-bred colt that was about 1 year old when it was used for anatomical dissection. The right testis was located in the scrotum and appeared to be normal. The left testis could not be seen nor palpated on gross examination. "Instead, a peritoneal ligament extended from the area of the vaginal ring forward to attach to the dorsocaudal angle of the spleen. . . The gubernaculum testis appeared to be well developed. The vas deferens appeared normal as it passed caudally from the area of the vaginal ring to the prostatic urethra, but was difficult to trace cranially toward the spleen" (Frandson *et al.*, 1960).

Histologic examination revealed the presence of "numerous testis cords like those one would normally expect to observe in the gonadal ridge of the developing male embryo. Some of the testis cords appeared to be developing a lumen, indicating their potential as convoluted seminiferous tubules. A few cells resembling the interstitial cells of Leydig were observed in the vascular areolar stroma." An epididymal duct and a ductus deferens were attached to the gonad.

Ectopic Adrenocortical Tissue

Nodules of ectopic adrenocortical tissue are frequently present on the lower part of the spermatic cord (Fig. 13.9), between the head of the epididymis and testis and in the mediastinum testis of horses. The ectopic tissue can be found most readily in young colts and in older horses that have been exposed to chronic stress. Nodules of ectopic adrenocortical tissue occur less frequently on the gonads of other species of domestic animals. Neoplasia of misplaced adrenocortical tissue has been reported in man but not in domestic mammals.

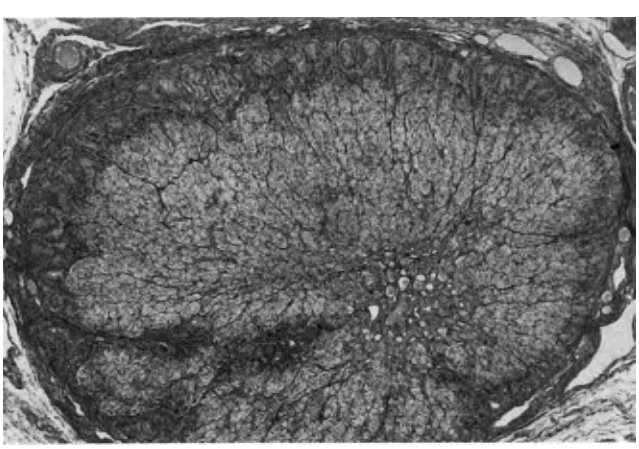

Fig. 13.9. Adrenocortical tissue on equine spermatic cord. ×9. Acc. No. 18985.

Ectopia Testis

In ectopia testis, the gonad fails to reach the scrotum and lies in a position other than in the normal line of descent. Herbut (1952) reported the following varieties of ectopia testis in man: interstitial (superficial inguinal), pubopenile, femoral (crural), transverse, perineal, and pelvic.

Pearson (1972) reported six cases of testicular ectopia in bulls. He stated that "four were in a pre-scrotal position along the ventral abdominal wall fairly close to the prepuce; the remaining two were on the inner aspect of the upper part of the thigh. All were subcutaneous, covered only by skin and a layer of connective tissue. . . . The testes were smaller than scrotal gonads but not markedly so."

Cysts of the Tunica Albuginea Testis

Cysts of the tunica albuginea testis are rare in domestic mammals. Arcadi (1952) reported three cases in men and concluded that "previous infection may well play an important part in the formation of cysts of the tunica albuginea testis." However, the etiology was not established. It is possible that the cysts were due to congenital malformation of the tunica albuginea testis.

Horizontal Testes in Bulls

Carl (1943) reported that two bulls each had one normally placed testis and one testis lying parallel to the abdomen. These bulls had the same grandsire.

Cryptorchidism (Retained Testis, Undescended Testis)

A cryptorchid testis is one that fails to complete its normal descent into the scrotum. The condition may be bilateral, but it is usually unilateral. The unilateral cryptorchid is sometimes referred to incorrectly as a monorchid. Cryptorchidism occurs most frequently in pigs and horses. It is uncommon in cats, sheep, and cattle.

Boar. Wensing (1968) proposed that there are three ways in which abnormality of the gubernaculum can affect testicular descent in the pig, including: "(1) absolute or relative failure of growth, (2) excessive growth, and (3) aberrant growth causing the gubernaculum to extend into an unusual position." The gubernaculum is a mesenchymal structure that extends from the caudal pole of the young fetal testis to a position just beyond the external inguinal opening. Wensing (1973) stated that "according to our studies, testicular descent is largely brought about by an increase in size of the extra-abdominal part of the gubernaculum (swelling reaction), whereby a tractive power is developed that moves the testis towards the inguinal canal. . . . In a survey of 1,750 male pig foetuses abnormalities in testicular descent were discovered that appeared to be caused by aberrations of gubernacular development."

1. Considerable underdevelopment of the gubernaculum of both testes was found in two fetuses. It was stated that "we have quite regularly seen foetuses in which development of the gubernacula was unequal although both fell within the normal range. Asymmetrical development of the gubernacula is even more common in the dog than in the pig" (Wensing, 1973).
2. Excessive growth of the gubernaculum was found in 20 fetuses. "By excessive growth, we mean that the gubernaculum exceeds the normal size for that age by a substantial margin, say more than 50%. About half of the 20 foetuses in this group had gubernacula that had developed in the normal direction, that is within the fascial pouch formed by the continuation of the external abdominal fascia and the aponeurosis of the external oblique muscle" (Wensing, 1973). These pigs would have descended testes, wider than normal inguinal canals, and be at increased risk for developing inguinal hernias. The animals with excessively large and abnormally located gubernacula would have retained testes.
3. In 42 pigs, the growth of the gubernaculum was normal or exaggerated, but it developed in an abnormal site direction. Thus, testicular descent was lacking or incomplete. "This finding is important because many workers are still convinced that the primary cause of incomplete descent is malfunction of the fetal or neonatal testis" (Wensing, 1973).

Wensing and Colenbrander (1973) described the postnatal events in 65 piglets with incomplete testicular descent. The abnormalities were classified as follows: high abdominal cryptorchidism, low abdominal cryptorchidism, inguinal hernia combined with eventually normal testicular descent, mal-location of the testis with the abdominal wall combined with inguinal hernia, and normal testicular location "finally established even when the neonatal status was abnormal in any of the ways described under low abdominal cryptorchidism." Wensing and Colenbrander (1973) stated that "as a crude guide, it can be said that when the neonatal gubernaculum is enlarged more than twice its size, both descent and hernia are probable."

Frankenhuis and Wensing (1979) demonstrated that spermatogenic arrest in the cryptorchid boar is not due to an inborn defect in the testis but is caused by maintenance of the testis at the abdominal temperature. They subjected the abdominal testes of adult, unilaterally cryptorchid boars to continuous artificial cooling for 5 to 45 days: "After a cooling period of 45 days, there was complete differentiation in many seminiferous tubules." Fredeen and Newman (1968) reported that 1 to 2% of all male pigs marketed in Canada have cryptorchidism. Inbreeding increased the incidence of the defect to as high as 50%. McPhee and Buckley (1934) concluded that cryptorchidism in swine is due primarily to the action of a single recessive gene.

Stallion. Wright (1963) reported 101 cases of equine cryptorchidism. The testes were in the abdomen in 50 horses and in the inguinal region in 51. In the abdominal cases, the tail of the epididymis occupied a short processus vaginalis in 10 horses, a teratoma was present in 5, and the testis was cystic in 2. He mentioned that "a striking feature of the abdominally situated testicle is that, apart from its 'head,' the epididymis is unattached to it; in fact, the 'tail' is some 3 or 4 inches away at the ring itself. . . . In the majority of cases, there is no processus vaginalis and the partial detachment of the epididymis allows the gland significant movement. In a minority of cases, a short processus occupies the canal, and when this is present, it is occupied by the tail of the epididymis which is attached to it by the gubernaculum" (Wright, 1963).

Wright described two types of inguinal cryptorchids in horses. In one type, the testis lies in the inguinal canal with the long axis disposed vertically and preceded by the tail of the epididymis. In the other type, "The testis has passed through the inguinal canal and lies at the external ring. It is larger than in the preceding type, and its long axis is horizontally disposed" (Wright, 1963).

Inexperienced surgeons sometimes remove the tail of the epididymis and a portion of the epididymal body and leave the testis and the rest of the epididymis in the abdominal cavity. Trotter and Aanes (1981) reported three cases of incomplete castration in cryptorchid horses that were examined during an 8-month period: "Each horse had had surgery to remove 1 retained testis. In each case, the attending veterinarian believed castration had been adequately completed." The horses continued to act like stallions following the initial incomplete surgery. One of the stallions was operated upon three additional times without locating testicular tissue. The horse was unmanageable for riding, thus the owner requested that the animal be killed. At necropsy, a 7 × 3-cm testis and the head and body of the epididymis were found to be suspended by a portion of the mesorchium and the spermatic cord. The testis and the remaining portions of the epididymis were removed from the other two horses during the second operation. The behavior of both stallions changed to that of a gelding within a few days following surgery.

Bergin *et al.* (1970) dissected 50 equine fetuses and 13 foals with normal and abnormal testicular descent. They stated that "the testis is surrounded by the peritoneal cavity, suspended from the dorsal body wall, by a broad thin mesorchium and is connected to the groin by the gubernaculum and posterior gonadal (epididymal) ligament. Expansion of the vaginal process around the gubernaculum because of continuous pressure of peritoneal fluids results in tension on the gubernaculum, drawing the testis to the internal inguinal ring. Enlargement of the gubernaculum and epididymal ligament stretches the inguinal canal, allowing passage of the testis through the canal, normally between 300 days of gestation and 10 days after birth."

Stickle and Fessler (1978) conducted a retrospective study of 350 cases of equine cryptorchidism. They found that left versus right testis retention was nearly equal. On the left side, 75.2% of the retained testes were located abdominally and 24.8% inguinally; on the right side, 41.8% of the retained testes were abdominal and 58.2% inguinal. One sustentacular cell adenoma and one teratoma were found in abdominal testes.

Cox *et al.* (1979) analyzed data collected during the examination of 500 cryptorchid horses. They stated that "left- and right-sided abdominal cases occur with approximately equal frequency in ponies. Approximately half the right-sided unilateral abdominal cases have the epididymal tail descended, while only 20% of the left-sided cases do. . . .Right-sided retention predominates in young ponies, probably being an extreme expression of testicular hypoplasia, but in older ponies and in other types of horses, retention occurs equally on the left and right."

Cox (1982) reported that "Scrotal testes in unilateral cryptorchids tend to be larger than those of normal stallions, sometimes exceedingly so, although occasional small scrotal testes are recorded. . . . Abdominal testes do not appear to increase in size with age, but if a unilateral cryptorchid has its scrotal testis removed, the remaining abdominally retained testis undergoes marked hypertrophy."

Crew (1922) reported dermoids (benign teratomas) in the testes of 4 of 15 cryptorchid horses. The average size of the retained testes was 5.75 × 4 × 4 cm. The sizes of the neoplastic testes were 7 × 5.5 × 5 cm, 12 × 9.5 × 5 cm, 7 × 5.5 × 5 cm, and 9.5 × 8 × 3 cm. The teratomas consisted of cartilage, bone, adipose tissue, fibrous tissue, cysts containing gelatinous material, glandular tissue, and hair.

The seminiferous tubules in retained testes are lined predominantly or entirely by sustentacular cell (Fig. 13.10). Calculi are occasionally present in the tubular lumina. The interstitial cells usually appear to be normal but occasionally give rise to neoplasms in old stallions.

Kumi-Diaka *et al.* (1981) diagnosed 74 (27%) cases of cryptorchidism during the clinical examination of 274 donkeys in Nigeria. Fifty of the 74 cases involved the left testis, 18 the right, and 6 were bilateral. The retained testes were located in the inguinal region. Three animals lacked a detectable scrotum. They stated that "These animals were uniformly aggressive, prone to biting and kicking, and all exhibited excessive libido."

Ram. Blackshaw and Samisoni (1967) reported some metabolic, enzymatic, and histochemical characteristics of scrotal and cryptorchid testes of Merino rams. The mean weights of the testis and epididymis of six cryptorchid rams were 19.2 and 5.8 g as compared to 194.3 and 35.4 g for the normal testis and epididymis, respectively. "Aerobically, both the normal and cryptorchid testes accumulated similar amounts of lactic acid, but anaerobically, glycolysis in the normal testis was inhibited, whereas in the cryptorchid organ it was stimulated" (Blackshaw and Samisoni, 1967). Dehydrogenase activity, as measured by tetrazolium reduction, was similar in the retained and descended testes. The histochemical activities of lactate and glucose 6-phosphate dehydrogenases were somewhat greater in the normal seminiferous tubules. "Acrylamide gel electrophoresis of tissue ex-

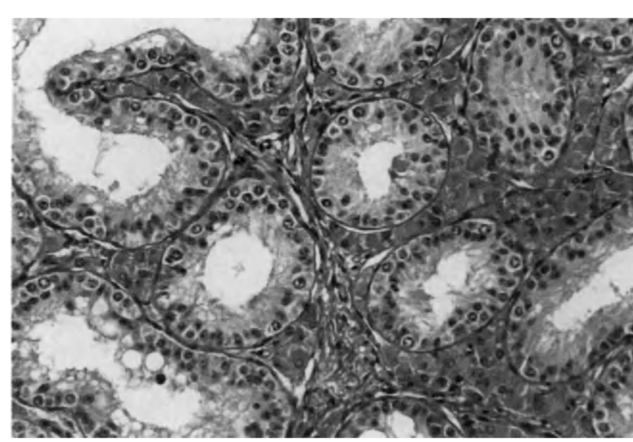

Fig. 13.10. Equine cryptorchid testis. ×222. Acc. No. 18774.

tracts showed the presence of a specific X (testis) isoenzyme of lactate dehydrogenase in the normal testis and in spermatozoa, which was absent from the cryptorchid testis and from skeletal muscle" (Blackshaw and Samisoni, 1967).

Dennis (1979b) conducted a survey of urogenital defects found during necropsies of 4417 lambs in Western Australia. Seventy male lambs had malformations of the reproductive organs. The animals with scrotal and/or testicular defects included 24 with partially cleft scrota, 15 with completely cleft scrota, 6 unilateral cryptorchids, 12 bilateral cryptorchids, 2 polyorchids, 1 monorchid, 1 with testicular and scrotal hypoplasia, 2 with scrotal hernias, and 3 male pseudohermaphrodites. Seven male lambs with defective genital organs also had renal malformations. Five of the cryptorchids had unilateral renal agenesis. One of the polyorchids had three testes, and the other had four testes.

Goat. Male pseudohermaphroditism is associated with cryptorchidism in polled goats and is discussed in Chapter 2.

Skinner *et al.* (1972) conducted a survey of the incidence of cryptorchidism in 7945 goats on 30 farms in South Africa. "Only three farmers reported no cryptorchids, and the average percentage was 1.98% with a maximum of 10%." They concluded that "From the results of our survey it would appear that inter-sexes are extremely rare in the Angora breed and that the chromosome picture of the cryptorchids is the same as that for normal rams."

Mathew and Raja (1978b) reported 33 (3.3%) cases of cryptorchidism in 1000 slaughter goats. The condition was unilateral in 27 bucks and bilateral in 6. "The right testis was always retained in unilateral cryptorchidism. In 28 (84.9%) cases, the retained testis was seen inside the abdominal cavity, while in one (3.0%) it was located in the inguinal canal. The remaining 4 testes (12.1%) were found below the skin, slightly posterior to the external inguinal ring close to the penis" (Mathew and Raja, 1978b).

Ezeasor (1985) reported that "Unilateral cryptorchidism is a common condition amongst the West African dwarf goats of South-Eastern Nigeria, with the right testis being constantly retained and abdominal in position."

Bull. Wheat (1961) described four cases of unilateral left-sided cryptorchidism in purebred Hereford bulls. Sufficient information was not available to determine the mode of inheritance. "The anomaly could have resulted from recessive gene action, but a slightly preferred hypothesis is that it was caused by a dominant gene with variable expressivity" (Wheat, 1961).

Cowie (1963) reported 76 bulls with one or both testes missing from the scrotum. In 50 animals the left testis was retained in the abdomen or inguinal canal, and the right testis was affected in 21 bulls. Four animals proved to have been born with only one testis. Of these, 3 had only a right testis, and 1 had only a left testis. One bull had both testes retained in the abdomen and did not show male aggressiveness until it was 22 months old. Regarding clinical diagnosis of cryptorchidism in the bull, Cowie stated that "Examination of the animal per rectum makes a diagnosis easy since the position of an abdominal testicle in the bovine animal is always close to the internal inguinal ring, and this testicle can be readily palpated through the rectal wall."

Hoffmann (1967) reported that a calf with 60, XY/62, XX chimerism had inguinal testes and shortening of the penis.

Dog. Pendergrass and Hayes (1975) reviewed the abstracts of 1266 cases of cryptorchidism in dogs seen at 12 veterinary schools that participated in the Veterinary Medical Data Program of the National Cancer Institute. The cases were identified from medical abstracts submitted from March 1964 through June 1974. The breeds at significantly high risk included the following: Chihuahua, Miniature Schnauzer, Pomeranian, Poodle (minature, toy, and standard breeds), Shetland Sheepdog, Siberian Husky, and Yorkshire Terrier. They stated that "Perhaps the breeds at high risk of cryptorchidism reflect the effects of a genetic mechanism. However, the wide breed distribution (68 individual breeds with at least 1 case) and the heterogeneous character of the breeds at high risk seem to indicate that inheritance is not the predominant mechanism." They reported that "hip dysplasia, patellar dislocation, defects of the penis and prepuce, and umbilical hernia were excessively associated with cryptorchidism. Testicular tumors were diagnosed 10.9 times more commonly among cryptorchid dogs." Seminomas and sustentacular cell tumors accounted for more than 97% of the testicular neoplasms of the retained testes.

In regard to canine cryptorchidism, Hutt (1979) stated that "This defect appeared at one time to provide a perfect example in the dog of a sex-limited hereditary condition. It may still do so, but there is now some question about the extent to which it is genetic in origin."

V. S. Cox *et al.* (1978) reported 12 cases of cryptorchidism in a colony of purebred and crossbred Miniature Schnauzers. Five cases were unilateral, and 7 were bilateral. All the ectopic testes, except one, were in the abdomen. The degree of inbreeding was greater for the bilateral than the unilateral cases. They suggested that a multiple gene defect was involved.

Rehfeld (1971) reported on cryptorchidism in a long-term study of Beagle dogs. He stated that "In many instances testicles did not descend into the scrotum until between four and six months of age."

Kawakami *et al.* (1988) investigated the effect of cryptorchidectomy on testicular function of the scrotal testes of six adult dogs with unilateral cryptorchidism. Prior to surgery, the testosterone level of testicular venous blood from the scrotal testes was lower than normal and there were fewer germ cells than in normal dogs. They reported that by 24 weeks following surgery the plasma testosterone levels and the number of germ cells were the same as those in normal dogs.

Cat. Bloom (1959) stated that according to his experience the incidence of cryptorchidism in the cat was about 0.75% and that it was more commonly unilateral than bilateral and abdominal than inguinal. The left testis was affected more frequently than the right.

Mason (1976) reported the occurrence of estrual behavior for 6 weeks in a 3-year-old bilaterally cryptorchid cat. The cat was castrated, and normal behavior resumed within 1 week. The author reported diffuse hyperplasia of the interstitial cells of the retained testis.

Testicular Microlithiasis (Testicular Intratubular Bodies)

Crew and Fell (1922) reported "ovum-like bodies" in the seminiferous tubules in the ectopic testis of a goat, cat, and rabbit. They stated that these bodies "proved to be not ovarian but the degeneration products of the germinal epithelium of the seminiferous tubules. The bodies appear to be produced by the gradual liquefaction of masses of desquamated cells, whereby large colloid globules are formed which subsequently undergo calcification."

I have seen similar structures in retained equine testes. Intratubular bodies in the retained testes of man have been reported by Bieger *et al.* (1965) and Nistal *et al.* (1979).

Testicular Hypoplasia

Testicular hypoplasia is a gross diagnosis that covers a number of underlying histologic changes, including germ deficiencies of various types, germ cell weakness, and spermatogenic arrest.

Testicular Hypoplasia in Swedish Highland Cattle (SKB—Swedish Polled Breed)

Swedish Highland cattle have classically been white with large areas of black and brown on the sides of the body and with black or brown ears and muzzle. At the turn of the century, breeders began to select animals with less pigmentation, resulting in predominantly white animals. The breeders soon noticed that along with the change in pigmentation, the left testis was smaller than the right in some of the bulls. The affected bulls were usually fertile, so little attention was paid to the difference in size of the testes, and affected bulls were extensively used for breeding (Lagerlöf, 1957a). In the early 1930s, it was observed that some bulls had bilateral testicular hypoplasia and were sterile. Thus, Lagerlöf (1938) and Eriksson (1943) began an investigation of the testicular defect in Swedish Highland cattle. Lagerlöf conducted clinical and pathologic examinations, and Eriksson pursued genetic studies. Sexual desire and serving ability are not affected, and secondary sexual characteristics are normal. It is the left testis that is usually hypoplastic, but occasionally the right testis or both are affected. The degree of hypoplasia in an affected gonad varies from partial to total.

Lagerlöf (1957a) stated that "A hypoplastic testicle in a sexually mature animal has a firmer consistency than a normally developed testicle, and the tail of the epididymis can be felt to be less distended and firm. In cases of bilateral hypoplasia both testicles are too small in relation to the bull's age." Eriksson (1943) reported that "Hypoplasia may affect either the left sexual gland, which is most common, or both sexual glands, which is less common, or the right sexual gland, which is rare. The frequency of the above-mentioned localization is in the ratio of 82.1 : 14.5 : 3.4. . . . the relation being approximately the same in both sexes."

In cases of total hypoplasia, all the seminiferous tubules are lined merely by sustentacular cells. In partially hypoplastic testes, some of the seminiferous tubules are devoid of germinal cells, and varying degrees of spermatogenesis are present in the rest of the tubules. Cases of total testicular hypoplasia can be recognized at an early age because of the small size of the affected testes that do not contain germinal cells (Figs. 13.11 and 13.12). However, cases of partial hypoplasia are not usually recognized until puberty, when the difference in size of the affected and normal testes becomes apparent.

Eriksson (1943) conducted a genetic study of the material from both males and females. He concluded that gonadal hypoplasia in the Swedish Highland breed is caused by a recessive autosomal gene with incomplete penetrance.

Testicular Hypoplasia in Other Breeds of Cattle

Testicular hypoplasia in cattle, other than in the Swedish Highland breed, is discussed separately because it has not been subjected to comparable scien-

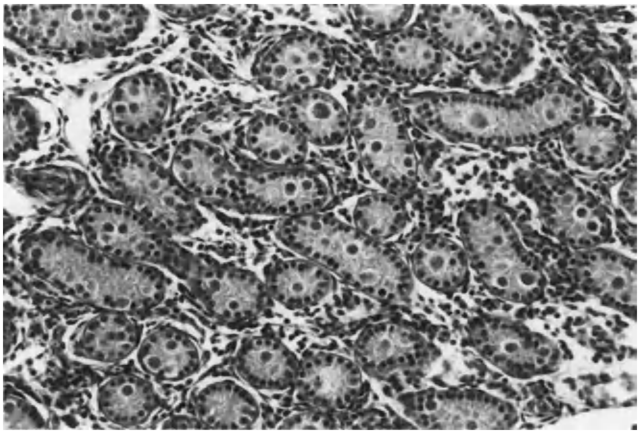

Fig. 13.11. Normal testis from a 1-month-old Holstein bull calf. The large cells in the tubules are germinal cells. ×81. Acc. No. 7600.

tific investigation. Thus, it is not known whether different types of hypoplasia are involved and whether they have different modes of inheritance. Korkman (1941) attributed the occurrence of testicular hypoplasia in an Ayrshire herd to genetic factors. Laing and Young (1956) reported the occurrence of testicular hypoplasia in 12 breeds of dairy and beef cattle in England and Wales. They stated that of the bulls examined for licensing in 1954, "Shorthorns may have had significantly more hypoplasts (.50%) rejected than Ayrshires (.26%), Friesians (.12%) and Herefords (.12%).... These figures may be biased because breeders may submit only those animals which they think are likely to pass the test. They do, however, suggest that the condition exists in many breeds, although at a very low frequency." In a series of 68 cases of hypoplasia, 49 were left-sided, 15 were right-sided, and 4 were bilateral.

Carroll and Ball (1970) investigated the effect of inbreeding on the occurrence of testicular lesions in beef bulls in Colorado. They found that inbreeding was associated with a significant increase in abnormal seminiferous tubules. "The incidence of abnormality increased as the level of inbreeding increased.... Testicular hypoplasia found in three different lines seemed to be of different types" (Carroll and Ball, 1970). They suggested that the hypoplasia in one line was similar to that associated with sticky chromosomes, and another was similar to the hypoplasia occurring with multipolar spindle formation in the spermatocytes. However, they did not use the techniques that Knudsen (1961a,b) used to identify these defects. Carroll and Ball concluded that "The relationship of the testicular hypoplasia in these bulls to the many affected bulls reported in the literature will remain obscure. The lack of a precise definition of the condition, as well as the non-specific changes observed in the testicles prepared by conventional histologic techniques, does not provide means for accurate comparison."

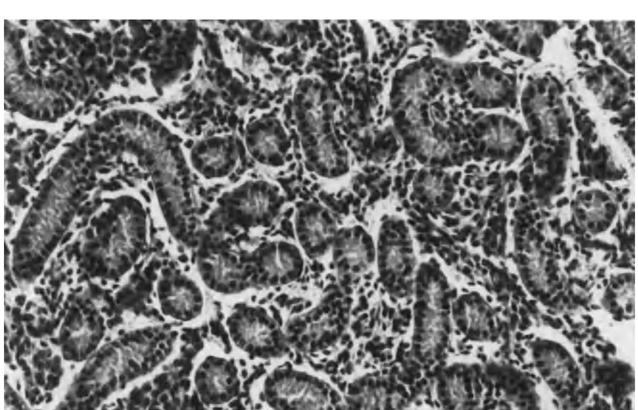

Fig. 13.12. Testis from a 1-month-old Swedish Highland calf with total testicular hypoplasia. No germinal cells were present in tubules. ×81. Acc. No. 14472.

Krishnalingam *et al.* (1982) conducted a quantitative macroscopic and histologic study of testicular hypoplasia in 17- to 23-month-old crossbred zebu bulls in Australia. The diameter of seminiferous tubules varied from 118 μm in bilateral hypoplastic testes to 171 μm in normal testes. "A mean tubule diameter of about 150 μm was considered useful for differentiating hypoplastic from normal testes in young post-puberal *B. indicus* crossbred bulls" (Krishnalingam *et al.*, 1982). They found a significant correlation between tubular diameter and sperm per gram of testis, suggesting that tubular diameter measurements in histologic sections could be used to predict sperm production. A compensatory increase in weight of the normal testis was noted in cases of unilateral testicular hypoplasia.

Total hypoplasia of the testis is relatively easy to diagnose on histologic examination. The seminiferous tubules are small, lined merely by sustentacular cells, and have a thin basement membrane (Fig. 13.13). Partial hypoplasia is more difficult to diagnose because many of the seminiferous tubules contain germinal cells and the condition may be confused with degeneration. In cases of partial testicular hypoplasia, some of the tubules are lined merely by sustentacular cells (Fig. 13.14), whereas in degeneration the tubules usually contain some germinal cells. In advanced testicular degeneration the basement membrane of the tubules is thickened.

Gonadal Hypoplasia (Low Germ Cell Resistance) in Swedish Red and White Cattle (SRB—Swedish Red Breed)

Lundgren (1972) reported the occurrence of gonadal hypoplasia in bulls and cows of the Swedish Red and

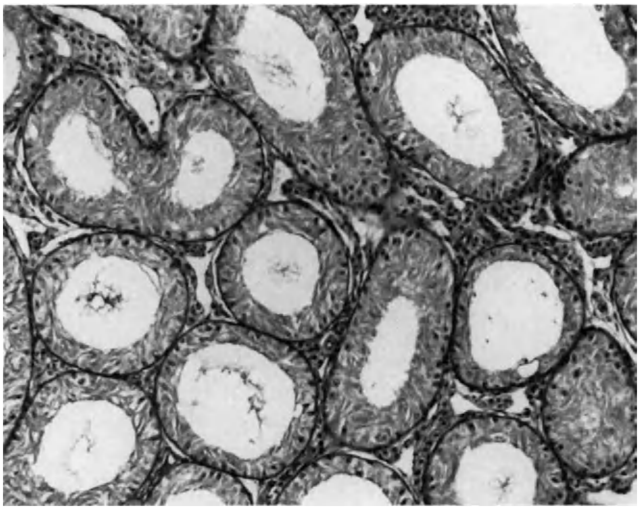

Fig. 13.13. Total testicular hypoplasia in a 19-month-old Holstein bull. ×81. Acc. No. 17882.

White (SRB) breed. I. Settergren (personal communication, 1975) refers to the condition as low germ cell resistance. The testes can be very small, but they vary in size up to normal. Spermatozoa are present in the semen, but they may be low in number. The development of spermatozoa may be abnormal, or they may have low resistance to storage or freezing. Sometimes the fertility is low in spite of normal-appearing semen. Although the defect occurs in both sexes, it appears to be more common in bulls.

In most of the affected bulls, the histologic lesions appear to be those of degeneration rather than hypoplasia. This is a progressive, uneven loss of germinal cells. Not all portions of the testes are affected to the same degree. The degenerative lesions appear to occur most frequently in the dorsal portion of the right testis. Thus, to establish a histologic diagnosis, it is necessary to examine tissue from at least three levels of each testis. In contrast to testicular hypoplasia in Swedish Highland bulls, the affected portions of the testes of Swedish Red and White bulls usually contain at least a few germinal cells (Fig. 13.15). Thus, it appears to be a focal degenerative process that generally occurs a relatively short time after the bull becomes sexually mature.

It is not known when the gonadal defect first appeared. Lagerlöf (1944) reported the occurrence of sporadic cases of gonadal hypoplasia in SRB cattle. Lundgren presented a brief discussion of the defect in 1972. He traced gonadal weakness in SRB cattle back to "545 Baven, one of the best progeny-tested bulls of the mid-1960's." Although this bull was of somewhat low fertility, 30 of his sons were selected for use in artificial insemination. Ten of his sons were of low fertility, and four were culled because of disturbances in spermatogenesis. One of his sons, 2 Fylla, was one of the outstanding bulls of the SRB breed, but he had a lower fertility than other bulls used for artificial insemination. Many of 2 Fylla's sons were selected for use in artificial insemination, but all of them were slaughtered when it became apparent that 2 Fylla was transmitting a gonadal defect.

Arrested Spermatogenesis in Swedish Friesian Bulls (SLB—Swedish Lowland Breed)

Arrested spermatogenesis was first reported by Lagerlöf in 1948 as testicular hypoplasia in the Swedish Friesian breed. It was found in line-bred bulls in the western part of Sweden. The condition was also described by Lagerlöf *et al.* in 1958. The gonadal defect occurs only in males.

Both testes are affected, and they are approximately of normal size in sexually mature young bulls. As the affected bulls grow older, the testes may be

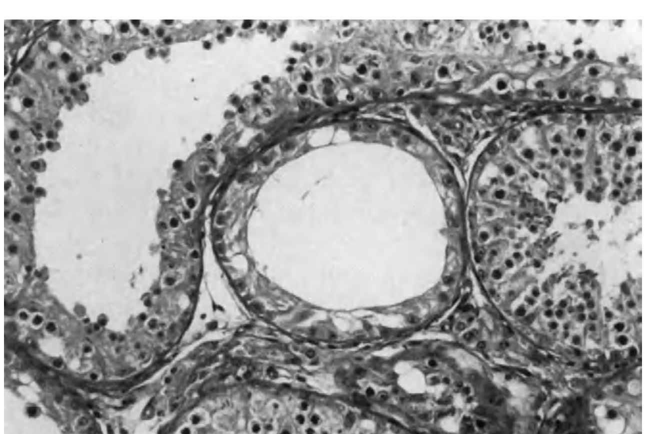

Fig. 13.14. Partial testicular hypoplasia in a 21-month-old Holstein bull. ×178. Acc. No. 19319.

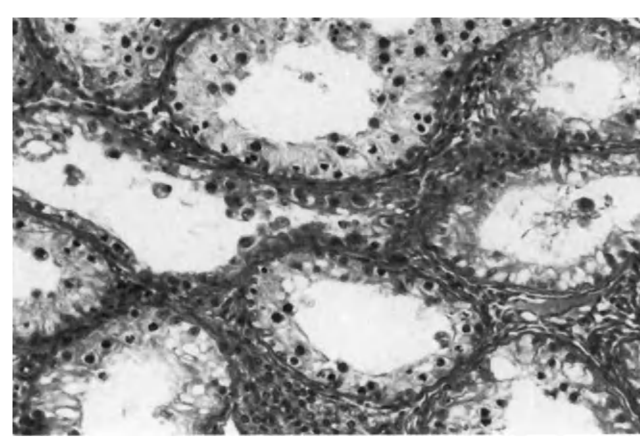

Fig. 13.15. Testis from a Swedish Red and White bull with low germ cell resistance. Note the marked loss of germinal cells. ×178. Acc. No. 13528.

smaller than normal. Libido is normal, and the ejaculates are watery. Multinucleated giant cells and free spermatids can be found in the centrifuged sample of the ejaculate. Histologic examination of the testis reveals that spermatogonia develop to spermatids, but there is almost no transformation of spermatids to spermatozoa. I have seen the defect in polled Hereford bulls (Fig. 13.16) in the United States.

Testicular Hypoplasia Associated with Sticky Chromosomes

Knudsen (1961a) reported the occurrence of sticky chromosomes associated with testicular hypoplasia in five highly inbred Holstein-Friesian (Swedish Lowland) bulls and in one Swedish Red and White bull. All the bulls had been mated to fertile cows but none sired offspring. The bulls had bilateral testicular hypoplasia and aspermia or oligospermia. The testicular weights ranged between 180 and 280 g. The consistency of the testes was normal, but the cut surface glistened somewhat more than normal. Knudsen stated that sediment from the centrifuged ejaculate "was dominated by pyknotic nuclei and to a lesser extent by hyperchromatic sperm-like bodies. In histological sections, pyknotic nuclei were evenly distributed throughout the seminiferous epithelium." Primary spermiocytes had "chromosomes in various stages of development and with abnormal or complicated bivalents or multivalents, free chromatin fragments, or with all the chromosomes gathered into a single chromatin mass. . . . Among secondary spermiocytes and spermatids, there is a tendency for cells of a given morphological type to form groups. The morphology of these cells varies widely from group to group, but the histologic appearance is dominated by karyolysis or karyopyknosis" (Knudsen, 1961a).

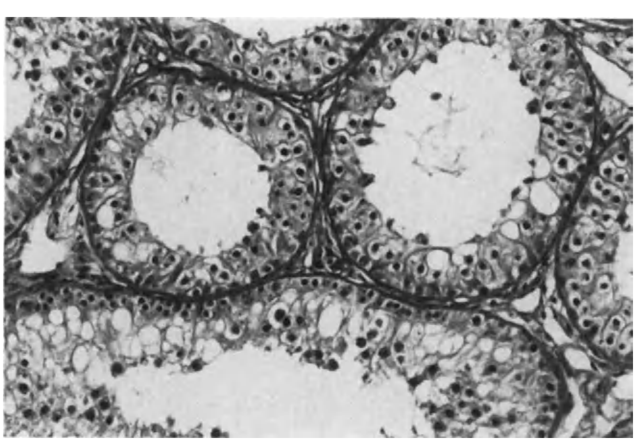

Fig. 13.16. Spermatogenic arrest in a 2 1/2-year-old polled Hereford bull. No spermatozoa were present. × 178. Acc. No. 15105.

These cells are the origin of the pyknotic nuclei present in the ejaculate.

Testicular Hypoplasia Associated with Multipolar Spindles in Spermiocytes

Knudsen (1961b) reported the occurrence of multipolar nuclear spindles in the testes of three highly inbred and closely related Holstein-Friesian (Swedish Lowland) bulls with arrested spermiogenesis. The bulls were rejected as breeders because of sterility or poor semen quality. They had moderate bilateral testicular hypoplasia, but the consistency of the testes was normal. Their libido was unusually strong, and they were difficult to restrain as they were led up to the teaser. The ejaculates were watery, and the volume varied between 1.5 and 5 ml. "If sperm were present at all, their number never exceeded 1,000/mm^3. The sperm concentration was too low to permit reliable estimation of the incidence of abnormal forms; most of those which could be seen were morphologically normal" (Knudsen, 1961b). A few viable giant cells were present in fresh unfixed smears.

The stained centrifugate of the ejaculate contained "giant cells of a particular appearance, as well as pyknotic nuclei, anuclear cell fragments, and a few sperm, usually normal. The giant cells with their two to more than 10 nuclei had a distinct cell membrane. Their nuclei varied greatly in size but were seldom larger than those of a spermatid." Nuclear morphology was often distorted as a result of degeneration. "As a rule, the nuclei were gathered in the center of the cells but occasionally filled out most of the cytoplasm" (Knudsen, 1961b).

Histologic examination of the testes revealed the presence of arrested spermatogenesis. The formation of multipolar spindles occurred during meiosis, and multinucleated cells were present in the later stages of spermiogenesis and in the ejaculate. According to Knudsen, "giant cells formed as a reaction to testicular degeneration have nuclei of a more homogeneous structure, usually located at the periphery of the cell. In bulls with multipolar nuclear spindles, the nuclei of the giant cells are flocculent and irregularly spaced in the center of the cell. Moreover, in these bulls the giant cells were abundant and were seen together with normal sperm in the centrifuged sediment of the ejaculate."

Sticky chromosomes and multipolar nuclear spindles are thought to be hereditary defects, but too few cases have been diagnosed to establish the mode of inheritance. Carroll and Ball (1970) reported cases of testicular hypoplasia in two inbred lines of bulls. They considered these to be similar to the cases of sticky chromosomes and multipolar spindle formation reported by Knudsen. However, they did not use the technique of semen examination nor the microscopic evaluation used by Knudsen (1961a,b). Thus, their diagnoses are tentative.

Testicular Hypoplasia Associated with Extra X Chromosomes (Klinefelter's Syndrome)

It has been reported that Klinefelter's syndrome affects between 1 in 500 (Centerwall and Benirschke, 1975) and 1 in 800 human males (Bishop, 1972). The condition is associated with the presence of more than one X chromosome. Bishop stated that in its most common form, "the chromosome complement contains the normal number of autosomes with the three sex chromosomes XXY. Rarer variants of the condition have other abnormal sex-chromosome constitutions such as XXXY, XXXXY, XXYY, and XXXYY and may display mosaicism of two or more lines of cells with different karyotypes, including the normal XY karyotype." A few cases with XX genotype have been reported. "Affected males remain more or less normal until the approach of puberty, but at that time the testes remain small and undergo striking degenerative changes with hyaline sclerosis and atrophy of the seminiferous tubules" (Bishop, 1972). The interstitial cells persist and make up the major portion of the testes. Adults are sterile but retain a male phenotype. Frequent features of the condition are mental retardation, abnormal breast development, underdeveloped secondary male characteristics, and a tall eunuchoid body. According to Bishop, "the incidence of Klinefelter's syndrome increases with increasing age of mother but appears to be independent of age of father, and in about 60% of the cases, the extra chromosome is believed to be maternal in origin."

Sterility associated with the XXY genotype in domestic male mammals has been reported in tortoiseshell and calico cats (Smith and Jones, 1966; Centerwall and Benirschke, 1975), the dog (Clough *et al.*, 1970), sheep (Bruère *et al.*, 1969a), swine (Breeuwsma, 1968), and cattle (Logue *et al.*, 1979). Mosaic variants of the genotype have been observed in the bull (Rieck *et al.*, 1969), boar (Harvey, 1968) and cat (Chu *et al.*, 1964; Biggers and McFeely, 1966; Smith and Jones, 1966; Loughman *et al.*, 1970).

Bishop (1972) stated that "Tortoiseshell cats have both yellow and black hair in the coat, either in discrete patches or intimately mingled to give a brindled effect, and the great majority are normal females. The expression of the yellow and black in the coat is controlled by a gene on the X chromosome which must be present in the heterozygous form for both colors to be expressed at the same time." Those in which the orange and black are mixed with white are called calico or tricolor cats.

There is a marked deficiency of germinal cells in the testes of animals with XXY testicular hypoplasia. All the germinal cells and many of the sustentacular cells eventually degenerate, leaving collapsed, hyalinized tubules and relatively numerous interstitial cells (Fig. 13.17).

Centerwall and Benirschke (1975) reported that "A review of the chromosome findings in 25 male tortoiseshell or calico (T–C) cats showed a variety of aneuploidy, polyploidy, mosaicism, and chimerism. An XXY-complement was included in the chromosome makeup of 16 of the 25 cats. Almost all of these cats were sterile. Testicular pathologic changes, when recorded, appeared comparable with that of human XXY Klinefelter's syndrome." They mentioned that the terms chimerism and mosaicism have been used interchangeably, but a clear distinction should be made. They defined a chimera as "an individual with cell populations of more than one genotype (karyotype) arising through a mixture of different zygotic genotypes, e.g., two separately derived genomes coexist in the same individual. (What would have been littermates fuse in early embryonic life to become one animal.) A mosaic is an individual with cell populations of more than one genotype derived from a single zygote genotype through mutational or zygotic events."

Long *et al.* (1981) reported that in the cat "When the present six cases are added to the 25 reviewed by Centerwall and Benirschke (1973), the most common chromosome complements are 39 XXY (19 percent), 38 XY/38 XX (19 percent), 38 XY/39 XXY (14 percent), and 38 XY/38 XY (11 percent). Of these, the 38 XY/38 XY animals have all been reported to be fertile. The 39 XXY have all been infertile, while fertility in the other groups has been variable."

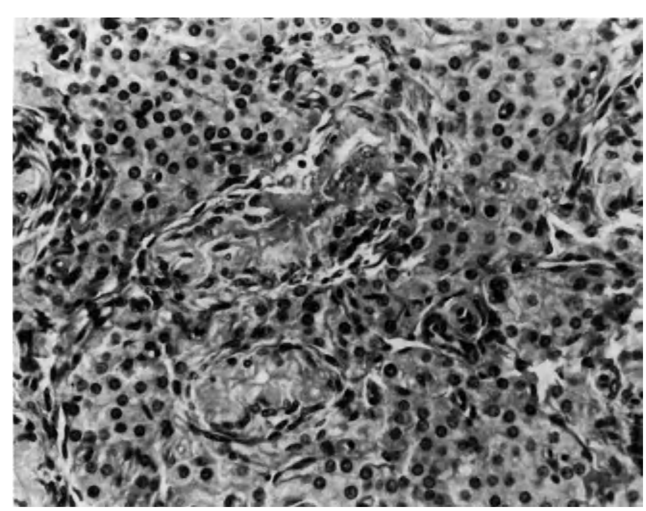

Fig. 13.17. Advanced testicular degeneration in an XXY bull. The seminiferous tubules are collapsed and devoid of germinal and sustentacular cells. ×204. Acc. No. 13837.

Testicular Hypoplasia in Goats

Testicular hypoplasia, other than that associated with pseudohermaphroditism (Soller *et al.*, 1963, 1969), has been reported infrequently in goats. Mathew and Raja (1978a) found 58 (5.8%) cases of testicular hypoplasia in 1000 slaughtered goats. The condition was bilateral in 56 bucks and unilateral in 2. "In bilateral hypoplasia the testicular size ranged from 2.2 × 1 × 1.4 cm to 3 × 2 × 2.2 cm and weighed 4 to 7.5 g."

Sponenberg *et al.* (1983) reported a case of testicular hypoplasia in a 1 1/2-year-old, 60,XY, Saanen goat. The left testis weighed 105.7 g and was considered to be of approximately normal size. The right testis weighed 51.5 g. "Pale translucent streaks radiated from the mediastinum into the testicular parenchyma of the right testis. No sperm granulomas were present in either testis or in the heads of the epididymides." Histologic examination revealed the presence of focal areas of seminiferous tubules lined merely by sustentacular cells (Fig. 13.18) at all levels of the testis. The adjacent tubules contained normal seminiferous epithelium. The left testis was histologically normal.

Testicular Hypoplasia in Sheep

Gunn *et al.* (1942) recorded unilateral testicular hypoplasia in Merino rams in Australia. They reported that this form of hypoplasia had a possible hereditary basis. Bruère (1970) stated that "In the ram, this is in fact probably the only reported form of testicular hypoplasia with evidence of an hereditary cause. That this type of hypoplasia is hereditary was based on the analogy with monorchidism and cryptorchidism, both of which are inherited in sheep (Warwick, 1931). Presumably the three conditions—monorchidism, cryptorchidism, and unilateral testicular hypoplasia—occurred together in the flocks examined by Gunn *et al.* (1942)."

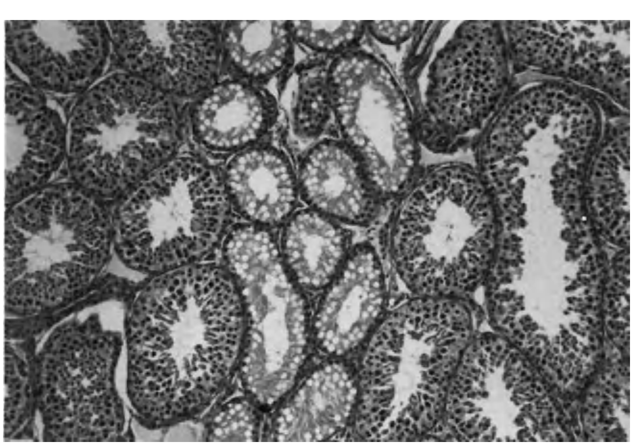

Fig. 13.18. Partial testicular hypoplasia in a goat. ×89. Acc. No. 19488.

Robertsonian Translocations and Testicular Anomalies in Sheep

There are conflicting reports on the effects of Robertsonian translocations on fertility in domestic mammals (Gustavsson, 1969; Pollack and Bowman, 1974; Bruère and Chapman, 1974; Bruère, 1974, 1975). Bruère and Mills (1971) reported that five rams in a pedigree flock had translocations and testicular abnormalities. Only three rams that were carriers of the translocation were known to be fertile. Two of the rams with testicular abnormalities had descent of only one testis, and "three had developed 'hour glass' testes with spermatogenic arrest." They stated that "The association of the testicular abnormalities . . . with the translocation may well be a chance phenomenon. It is possible, however, that the testicular abnormality (the 'hour glass' testes) may be the result of a gene effect which prevents the complete development of tunic vaginalis testis." A ram with the same testicular defect and normal karyotype was seen in another flock.

Testicular Hypoplasia in Swine

Holst (1949) reported testicular hypoplasia in six young boars that had very low fertility or were sterile. The boars came from herds where a number of other males were culled when young because of sterility. The weights of individual testes ranged from 200 to 275 g. The average weight of the right testis was 226 g, and the left weighed 240 g. "The histological examination shows a partial hypoplasia of varying degree in some seminal ducts with only one cell layer on the membrana propria and in other ducts disseminated degenerative changes in the seminal epithelium" (Holst, 1949). The diagnosis of testicular hypoplasia was made on the basis of breeding history of the boar, clinical examination, the low weight of the testes, and the histologic appearance of the testes.

Testicular Hypoplasia in Other Species of Domestic Mammals

Very little has been published on the pathology of testicular hypoplasia in the horse, dog, and cat except for the testicular lesions in the tortoiseshell and calico cats. Arthur (1975) stated that "In a large number of cases of equine hypoplasia seen by the author the right testicle was affected and the relatively high incidence of this condition in the Welsh Mountain pony breed, especially among the descendants of a particular sire (Boundy, 1970) indicates an hereditary origin."

Sterility in Hybrids

Hybrids develop from crosses between different animal species, and many have been described in a review by Gray (1972). The best known and most useful hybrids are the mule and hinny, which are the offspring of a male donkey and a mare and a stallion and a female donkey, respectively. The offspring of these matings are known for their hardiness, but the males have spermatogenic arrest and are sterile. The female offspring are also sterile. According to Benirschke (1967), "The only equine hybrid with attested fertility whose parental chromosome number and structure differed is the Przewalski's and domestic horse cross (Frechkop, 1964)."

Basrur (1969) reviewed the literature concerning cattle–bison hybrids. Cattalos have been defined as the progeny of crosses in which both parents are part bison and part cattle. Domestic cows that are mated with bison bulls frequently have excessive accumulation of fluid in the fetal membranes with a high mortality of the cows and calves. The reverse cross is more successful, but females predominate in the F_1 progeny. Basrur stated that "Although the F_1 male hybrids and the first back-cross males were consistently sterile, a small percentage of males with varying degrees of fertility were obtained in the subsequent back-cross generations. However, when the proportion of bison parentage was increased to over 14 by mating the cattalos with cows from F_1 or back-cross progenies the male cattalos were invariably sterile, whereas the females from such crosses were generally fertile." The sterile males had testicular hypoplasia.

Cystic Rete Testis

Gelberg and McEntee (1983) reported single cases of cystic rete testis in a cat and a fox. The feline case was diagnosed following routine castration of an 8-month-old domestic cat. A 9 × 16-mm cyst was noted in the head of the right epididymis. Both intact testes and epididymides were fixed in 10% formalin. "A mid-sagittal cut made through both testes and epididymides revealed that approximately 50% of the right testis was occupied by an irregular-shaped cyst with strands of tissue extending across the cyst." The cyst extended into the efferent ductules, which were distended with sperm in some areas. No sperm were found in the epididymis. "It appeared that efferent ductules became distended with sperm because they failed to communicate with the epididymis. While there were focal areas of degeneration of the seminiferous epithelium, active spermatogenesis was present in the majority of tubules" (Gelberg and McEntee, 1983). The cyst in the testis originated from the rete testis and that in the epididymis from the efferent ductules of the testis. The left testis and epididymis were normal. The other case occurred in a 10-year-old red fox with a seminoma. The tumor may have caused blockage of the excurrent duct system.

Inguinal Hernia

Wright (1963) reviewed the pathologic conditions of the inguinal canal including inguinal hernia, imperfect testicular descent, and other abnormal conditions of the canal, such as sequelae to castration and neoplasia of the inguinal lymph nodes. He reported that the incidence of congenital inguinal hernia is high in the pig, low in the foal and puppy, and rare in the calf and lamb. Wright stated that "In the congenital type, a large inguinal ring and a voluminous vaginal sac are developmental abnormalities, and while it is uncommon for the hernia to be present at the time of birth, it is well developed within a few weeks of postnatal existence. The hernia is generally a large one extending into the scrotum and involving a considerable length of small intestine, while its shape will vary according to the normal position of the scrotum relative to that of the inguinal aperture in the particular species." The condition may be unilateral or bilateral, and strangulation of the herniated intestine is rare. Inguinal hernias occur in intersex pigs, as well as in otherwise normal male pigs.

Wright found that acquired inguinal hernias occur most frequently in the stallion and ram, very occasionally in the bull and very rarely in other species of domestic mammals. He stated that "Acquired hernia of the adult stallion is entirely the outcome of some gross increase in intra-abdominal pressure with rupture of the deep transverse fascia which serves to close the gap between the anterior wall of the canal and the inguinal ligament. This would also explain the tendency to rapid strangulation which is a feature of the condition in the stallion" (Wright, 1963). There are a few reports of inguinal hernia in the gelding.

Acquired inguinal hernia is relatively common in the ram. Orr (1956) reported that in some flocks at least 5% of rams are affected. He believed that the condition was due to fighting when large groups of young rams were kept in closed sheds. Orr stated that "One has only to witness the head-on collision of two arrogant Blackface tups to appreciate the extent of the intra-abdominal pressure resulting." The hernia is usually unilateral, and the right side is most commonly affected. Usually only omentum is involved, but in some cases small intestine is also herniated.

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Chapter 14

Scrotum, Spermatic Cord, and Testis: Degenerative and Inflammatory Lesions

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- Traumatic Injuries
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Bibliography

Scrotal Lesions

Inflammatory Lesions

Inflammation of the scrotal skin elevates the temperature of the testes and causes testicular degeneration. Severe scrotal dermatitis, due to bacterial infection, occurs in bulls kept in filthy quarters. They have poor semen quality owing to secondary testicular degeneration, but semen quality usually returns to normal after the dermatitis is eliminated. Some of the specific causes of scrotal dermatitis in ruminants include *Dermatophilus congolensis, Besnoitia besnoiti, Chorioptes bovis, Haematopinus eurysternus,* and *Linognathus pedalis.* Cooper (1967) reported scrotal dermatitis due to *Tunga penetrans* in the boar.

Traumatic Injuries

Penetrating wounds of the scrotum may result in bacterial periorchitis. Scars remain in the scrotal skin in the previously traumatized areas.

Frostbite

Faulkner *et al.* (1967) reported that scrotal frostbite developed in 14.4% of 6389 bulls during a severe blizzard. Many of the affected bulls had unsatisfactory semen quality. "Mating behavior was adversely affected by severe lesions in some bulls. Older bulls with pendulous scrotums were more frequently and severely affected. . . . Semen quality improved in some affected bulls, but prognosis was unfavorable when there were testicular adhesions."

Varicose Veins

Varicosities develop in the veins in the lower part of the scrotum in some mature and aged bulls (Fig. 14.1). Some of the affected bulls have decreased fertility during hot weather.

Bloom (1954) reported that "Variocosis of the scrotum is not uncommon in older dogs. Grossly, there occur slightly elevated, somewhat flattened, multiple, focal, irregular thickenings of the scrotal

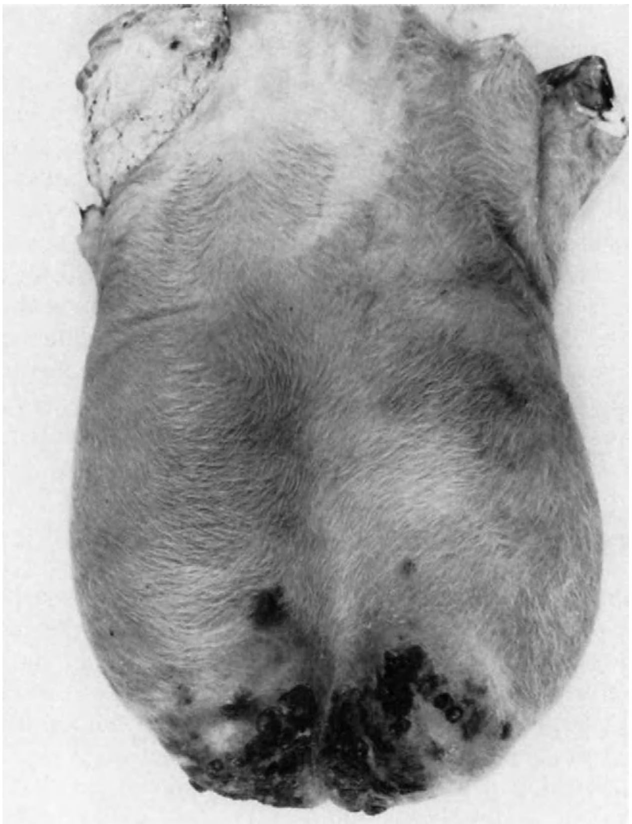

Fig. 14.1. Varicose scrotal veins from a 10 1/2-year-old bull. Acc. No. 9024. (Figs. 14.1, 14.3, 14.14, and 14.22 from Jubb and Kennedy, 1970.)

skin. These areas may be minute or several millimeters in size. The covering epithelium may be intact or ulcerated; in the latter, oozing of blood is observed in the living animal."

Lesions of the Spermatic Cord

Torsion of the Spermatic Cord

In the veterinary literature, torsion of the spermatic cord is frequently referred to as testicular torsion. The usual term for the condition is a misnomer because the primary lesion is in the spermatic cord. Twisting of the spermatic cord obstructs the blood supply to the testis and causes testicular necrosis. The condition occurs most frequently in the dog.

Horney and Barker (1975) described a case of torsion of the spermatic cord in a 2-year-old Standardbred stallion that was in training for a race. There was evidence of pain after a morning workout, and the owner noticed enlargement of the right half of the scrotal content. The evidence of pain persisted for 3 days and then subsided. The stallion then appeared normal except for the unilateral scrotal enlargement. Elective surgery was performed on the sixth day. The right testis and spermatic cord were rotated, and the cord was pulsating above the twisted area. The testis and epididymis were enlarged, deep red-brown, and surrounded by serosanguinous fluid. Unilateral castration was performed. Histologically, the testis and epididymis were congested and necrotic.

Pascoe *et al.* (1981) reported a 360° torsion of the left spermatic cord in a 2 1/2-year-old Quarter Horse. The predominant clinical sign was abdominal discomfort. The scrotum was moist and edematous, and "The left testicle was enlarged, firm and retracted slightly toward the abdominal cavity. . . . The tail of the epididymis and an elongated portion of the body of the epididymis were attached to the left testicle by an unduly long mesorchium. The caudal ligament of the epididymis and the proper ligament of the testis were elongated. These anatomic variations may have predisposed to torsion of the spermatic cord" (Pascoe *et al.*, 1981). The horse was a left-sided cryptorchid as a yearling, but the testis had descended into the scrotum when it was 2 years old. The loose attachment of the tail and body of the epididymis was probably associated with cryptorchidism in early life.

Pearson and Kelly (1975) reviewed 9 published cases of testicular torsion in dogs and described 13 additional cases. All of the 9 previously published cases occurred in cryptorchid testes, and 5 were in dogs between 5 and 15 months of age. Two of the older dogs had neoplasms in the twisted testes. The affected gonads in the 13 cases observed by Pearson and Kelly were intraabdominal in 11 dogs, in the inguinal region in 1 animal, and in the scrotum in the other. "Nine animals were presented with an acute illness characterized by anorexia and often associated with vomiting. . . . In eight of the cryptorchid animals, a painful mass was palpated in the posterior abdomen, and in two cases the abdomen was grossly distended" (Pearson and Kelly, 1975). Most of the 13 cases of torsion appeared to be a sequel to neoplastic enlargement of a retained testis.

Hulse (1973), Zymet (1975), and Young (1979) reported cases of torsion of fully descended testes in dogs. Young suggested that intrascrotal testicular torsion in the dog might be due to trauma resulting in rupture of the scrotal ligament. "Partial rupture of this ligament between the proper vaginal tunic and the spermatic fascia would allow a limited degree of torsion of the proper vaginal tunic and testicle. Rupture between the epididymis and tunic would permit a full range of torsion of the testis with the tunic" (Young, 1979).

Klingerman and Nourse (1967) stated that in boys, "torsion of the spermatic cord is a commonly misdiagnosed surgical emergency. . . . Our personal observations of torsion of the spermatic cord and the testicular appendages have impressed us that torsion is by no means rare and that the poor salvage rate is, in great part, attributable to misdiagnosis, culminating in inevitable infarction, and loss of the testis."

Varicocele

Very few reports of varicosity of the veins in the spermatic cord in domestic mammals have been published. Varicoceles frequently undergo thrombosis (Fig. 14.2). The condition occurs most often in the ram and is relatively rare in the bull. Gunn *et al.* (1942) mentioned that bilateral varicoceles are relatively common in Merino rams. They did not mention any effect on testicular function or fertility. Watson (1974) reported a case of bilateral varicoceles associated with testicular degeneration in a ram. Watt (1978) found varicoceles in 47 of 2281 Merino rams. The condition needs to be studied in more detail in domestic mammals.

Varicocele has been studied much more extensively in man than in domestic mammals. Steeno *et al.* (1976) reported that 11.7% of 20,362 patients in fertility clinics had varicoceles. They stated that it seems likely "that a varicocele starts at puberty and tends to attain a certain degree at the age of 14 years, with slow increase in severity during the years later on." They found that 93.9% of affected schoolboys and 78.3% of affected college students were not aware of the presence of the condition.

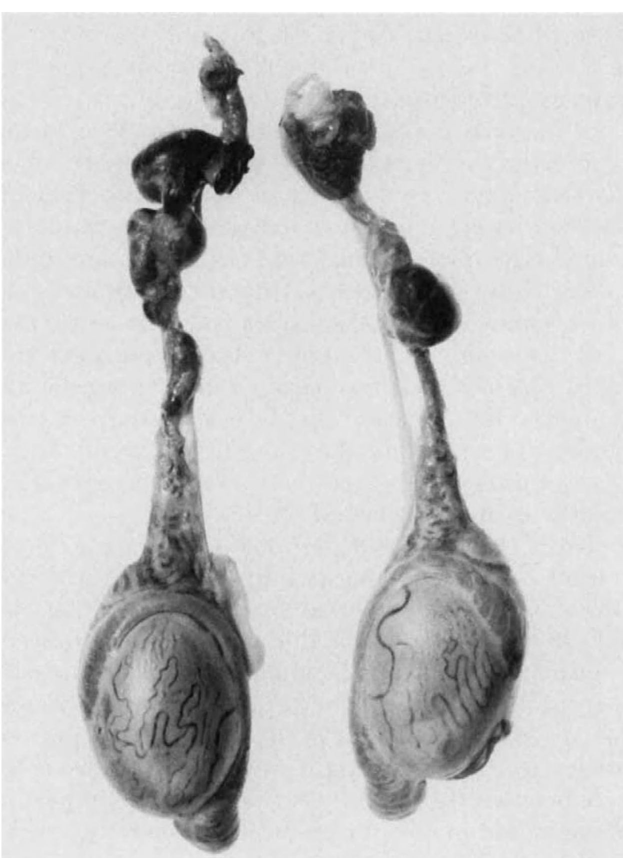

Fig. 14.2. Thrombosed varicoceles in the spermatic veins of an aged ram. Acc. No. 9062.

MacLeod (1969) reported that in man, "Varicocele is found almost invariably in the left scrotum, and it has been shown that ligation of the left internal spermatic vein not only results in disappearance of the varicocele, but in a good percentage of cases a marked improvement in semen quality may appear within a few months after the operation."

Spermatic Arteriovenous Anastomosis

David and McCullagh (1978) reported a case of spermatic arteriovenous anastomosis in a 5-year-old horse. The animal was purchased as a gelding, but it showed masculine behavior in the presence of mares. The owner mentioned that "the horse could not stand on 3 legs for any length of time. When being shod, it had to be held up and pushed against the wall in order to stop it falling over." The horse started swaying, and this continued when the foot was put down.

Numerous scars were found in the scrotal area, indicating previous surgery. Exploratory surgery revealed that the right testis had been removed and that the left testis was in the abdominal cavity. The spermatic cord consisted of a large mass of pulsating vessels. The vascular mass was too large to be removed through the inguinal canal, "so the abdominal cavity was entered through a ten cm paramedian incision just cranial to the earlier inguinal incision on the left side" (David and McCullagh, 1978). The testis and the mass of pulsating vessels were brought out through the incision. The vessels were ligated, and the spermatic cord was severed.

They reported that "The specimen is best described as an irregular contorted mass of large blood vessels attached to a small retained testis. The mass measured 20 × 20 × 15 cm, and testis, 10 × 5 × 2 cm. . . . The main artery, which connected the mass with abdominal aorta, measured 1.5 cm in diameter and coiled in a tight spiral. An even larger vein, measuring 3 cm in diameter, carried blood away from the lesion into the caudal vena cava" (David and McCullagh, 1978). A tangled mass of anastomosing blood vessels was located between the two major vessels. Most of the vascular mass was composed of vessels with an arterial structure, and their lumina became progressively smaller as the vessels approached the testis. There was a transition to venous structure when the mean luminal diameter was about 0.25 mm. The "blood channels became widely dilated, and their walls became thin and fibrous." There was no evidence of necrosis in the testis.

By 6 months following surgery, the horse had improved considerably. "It appears that the large apparent anastomosis of the spermatic artery was acting as a shunt and diverting a considerable part of the blood supply away from the hindquarters."

Occlusion of the Spermatic Cord

Dorn (1978) reported a case of occlusion of the spermatic cord by a herniated mass of omental fat. The dog was submitted to surgery within 12 hours after marked swelling of the left testis was first noticed. The hernia was corrected, and the testis returned to approximately normal size within 10 minutes. Neoplasms of the spermatic cord may cause occlusion of the vessels and infarction of the testis, especially in dogs.

Complications following Castration

Young horses can be castrated by using an emasculatome, and infections of the spermatic cord are usually avoided. When stallions 3 years of age and older are castrated, controlling hemorrhage is a more serious problem and ligatures are often used. Infections of the spermatic cord are more common when nonabsorbable suture material is used, but "even catgut ligatures are capable of provoking a persistent streptococcal infection of the cord, giving rise to the lesion French observers in the past called champignon" (Wright, 1963). The first sign of a problem is the presence of a blood-stained discharge from the wound 8 to 12 days following surgery. The remnant of the distal part of the spermatic cord becomes swollen and turgid. Abscesses develop later.

Wright (1963) stated that "Scirrhous cord differs from champignon in that it results from a chronic, low-grade, staphylococcal infection of the cord, giving rise to multiple and often quite small abscesses, surrounded by a progressively increasing mass of fibrous tissue which merges in an ill-defined manner into the surrounding connective tissue. . . . A striking feature of scirrhous cord is that, while it is sometimes recognized within a few months of castration, more often a much longer period, often several years, elapses before attention is drawn to it, and then generally as the result of hind-leg lameness due to the pain caused by a flare-up of infection." Now the condition occurs rarely.

Other complications that may follow castration include severe hemorrhage, excessive swelling of the surgical site, and evisceration of an inguinal hernia (Turner and McIlwrath, 1982). In cases of equine cryptorchidism, the body and tail of the epididymis may be attached loosely and located some distance from the testis. Inexperienced surgeons occasionally remove the epididymal tail and leave the rest of the epididymis and testis in the abdominal cavity. Major surgery is then required to remove the retained testis. I know of one case in which three operations were performed to remove a cryptorchid testis from a horse. The tail of the epididymis was removed first, then the body of the epididymis was removed during the second operation, and finally the head of the epididymis and testis were removed during the third operation.

Pearson (1972) reported a variety of complications following improper castration of 12 bulls. Three developed hematomas and infection of the spermatic cord following open castration. The other complications followed improper use of elastrator bands and burdizzo forceps. Elastrator bands were placed below the testes in three bulls, and the gonads continued to grow. They were eventually castrated surgically. Two bulls each had the following complications after the use of Burdizzo forceps: occlusion of the urethra, testicular abscesses, and unsuccessful castration leaving viable testicular tissue.

Caseous Lymphadenitis

Williamson and Nairn (1980) reported that 8% of 200 rams had *Corynebacterium pseudotuberculosis* infection in the scrotum. The lesions were generally located "high in the neck of the scrotum, in the fascia adjacent to, but separate from, the spermatic cords. . . . The lesions ranged from 2 cm to 8 cm in their largest dimensions, and were firm, generally ovoid and smooth or occasionally lobulated." The lesions consisted of encapsulated caseous abscesses that apparently developed in the superficial (external) inguinal lymph nodes. A few lesions may have developed in testicular lymph nodes on the spermatic cord.

Lesions of the Appendix Testis

The appendix testis is a vestigial remnant of the proximal part of the paramesonephric duct. It is a pedunculated structure located on the testis near the head of the epididymis.

Torsion of the Appendix Testis

In the human male, especially in young boys, the appendix testis may undergo torsion and cause considerable pain (Skoglund *et al.*, 1970a). In some horses that suddenly become lame, pain seems to be referred to a testis and may be due to torsion of the appendix testis. However, as far as I know the condition has never been diagnosed clinically nor during postmortem examination of stallions. I believe that it occurs because the appendix testis is usually a relatively tall structure in young animals and is frequently a flattened mass of tissue in old stallions. A careful search of the scrotal contents in old stallions might reveal the presence of necrotic, detached portions of the appendix testis.

I have seen only one case of torsion of the appendix testis, and that occurred in a goat. The torsion apparently happened a relatively short time before castration because the hemorrhagic, necrotic portion of the appendix was still attached to the testis.

Strongyle Lesions in the Appendix Testis

Strongylus edentatus larvae frequently migrate to the testis and cause focal granulomatous lesions in the testicular tunic (Fig. 14.3). They sometimes invade the appendix testis and cause hemorrhagic lesions that, on superficial examination, may resemble torsion of the appendix. Hemorrhage, inflammation, and squamous metaplasia occur as a result of the larval invasion. The parasitically induced metaplasia has been misdiagnosed as squamous cell carcinoma.

Lesions of the Appendix Epididymis

The appendix epididymis is a vestigial remnant of the embryonic mesonephric duct. Cysts and torsion of the structure have been reported in man, but only cysts have been seen in domestic mammals. They occur occasionally in all species of animals. The cysts are usually located between the head of the epididymis and the testis but are present occasionally on the surface of the testis adjacent to the head of the epididymis. Very large cysts may be present between the epididymis and testis in older animals. They do not interfere with the function of the epididymis because they enlarge very slowly over a long period of time and do not block the movement of sperm.

Fig. 14.3. Migration tract of a strongyle larva covered by fibrin on the surface of an equine testis. The lesion is located adjacent to the epididymis and includes the appendix testis. Acc. No. 13602.

Lesions of the Tunica Albuginea

Cysts of the Tunica Albuginea

Cysts of the tunica albuginea testis are rare in domestic mammals and in man. Arcadi (1952) reported three cases in man and stated that the lesion was not mentioned in a number of classic urology texts. The etiology of the cysts was not determined with certainty. Arcadi concluded that inflammation was a more likely cause than congenital malformation of trauma.

Adhesions of the Tunica Vaginalis

Adhesions between the parietal and visceral layers of the tunica vaginalis are very common in bulls and rams. Fine, fibrous adhesions are found mainly in the region of the epididymal tail and are of no clinical significance. The etiology of these fine tags of fibrous tissue has not been established. Widespread, dense adhesions may be associated with testicular degeneration (Lancaster, 1956) and may possibly be due to trauma (Galloway, 1961). The incidence of adhesions increases with advancing age. Burgess (1983) found adhesions in 124 (22%) of 553 rams.

Hydrocele and Hematocele

These lesions are comparatively rare in domestic mammals. The reason for the more frequent occurrence of hydrocele in man than in animals is that the communication between the testicular and peritoneal cavities closes in man and remains open in most domestic mammals.

Hematocele may be due to traumatic injury to the testis or secondary to hemorrhage in the peritoneal cavity.

Lesions in Regional Lymph Nodes

Animals with orchitis and epididymitis have inflammatory lesions in the lymph nodes that drain the testis and epididymis. Vasectomized animals and those with sperm granulomas in the testis and epididymis develop sperm granulomas in the regional lymph nodes (Ball and Setchell, 1983).

Testicular Lesions

Testicular Biopsy

Testicular biopsy has been used more frequently by urologists for studying infertility in man than it has been by veterinarians for studying infertility in domestic mammals. One of the primary reasons for the failure of the technique to be accepted as a diagnostic procedure in domestic mammals is that much of the experimental work has been done in the bull, and the results have been very unsatisfactory. The bovine testis has a very thick tunica albuginea with a rich vascular network. If one of the large vessels in the tunica albuginea is cut, hemorrhage and infarction develop and cause severe testicular degeneration (Figs. 14.4 and 14.5).

The majority of reports concerning testicular biopsy in bulls indicate that a marked decrease in sperm concentration occurs following the operation. If the procedure is conducted with care in the bull, avoiding the highly vascular areas and suturing the incision so that the hemorrhage and adhesions do not develop, the technique can be used successfully.

Fig. 14.4. Infarction of bovine testis and sperm stasis in many of the adjacent seminiferous tubules following removal of tissue for biopsy. Acc. No. 2389.

Fig. 14.5. Shrinkage of the right bovine testis following surgical removal of a piece of tissue from the ventral part of the gonad. Severe hemorrhage occurred during the surgery, and it was controlled by compressing the spermatic cord. This caused infarction of the entire testis. Both testes were the same size prior to surgery. Acc. No. 1505.

In man the tunica albuginea is comparatively thin, and it is easy to avoid large vessels when the tunic is incised. By gentle compression of the testis, testicular tissue will bulge through the incision. This tissue can be incised with a sharp instrument, causing relatively little damage to the testis.

In the rabbit and dog, testicular tissue may be removed for biopsy with a minimal amount of damage. As in man, these species have a relatively thin testicular tunic, and the large vessels in the tunic can be avoided. If an attempt to control hemorrhage is made by grasping the spermatic cord or if the cord is stretched, there will be an interference with blood flow to the testis, and testicular degeneration will result. Hemorrhage should be controlled locally at the site of the incision.

Testicular Degeneration

Setchell (1978) reviewed the literature and presented an extensive bibliography on induced and naturally occurring degenerative lesions of the testis. A wide variety of etiologic factors may be involved, and in naturally occurring cases, the etiology is seldom established. Neumann *et al.* (1976) reviewed the effects of pharmaceutical compounds on male fertility.

Testicular degeneration may be focal or diffuse and unilateral or bilateral depending on the etiology. Gross lesions are not evident in mild to moderate cases of testicular degeneration. In cases of advanced degeneration, the testes are softer than normal and reduced in size.

The histologic lesions of testicular degeneration are usually nonspecific, and all testes have focal areas of germ cell death. Thus, the theoretically possible number of spermatozoa is never produced. Early degenerative lesions consist of the loss of scattered primordial germ cells, which may be discarded as individual cells or as multinucleated giant cells (Fig. 14.6). Vacuoles are present in areas from which necrotic germ cells have been discarded. Sperm frequently accumulate in seminiferous tubules near the rete testis in tubules with more advanced degenerative lesions. Calcium is deposited in these tubules with sperm stasis (Fig. 14.7). There is an increased loss of germinal cells (Fig. 14.8) as the degenerative process proceeds. Advanced degeneration can be differentiated from testicular hypoplasia by the increased thickness of the basement membrane in the degenerated testis (Fig. 14.9). In very advanced degeneration, the sustentacular cells, as well as the germinal cells, are lost. The affected tubules consist of thick, wrinkled layers of stromal cells (Fig. 14.10). The endocrine interstitial cells degenerate following the loss of the sustentacular cells.

Causes of Testicular Degeneration

Heat. Insulating the scrotum to prevent normal heat loss results in testicular degeneration in domestic mammals (Moore and Oslund, 1924; Glover, 1955). Heat-induced testicular degeneration occurs as a consequence of a number of factors—including fever, high environmental temperature, severe scrotal dermatitis, scrotal insect bites, blistering agents applied to the hocks of horses and bulls, accumulation of scrotal fat, edema and hematomas of the scrotum, unilateral orchitis or periorchitis with degeneration of the opposite testis, and severe systemic disease.

Setchell (1978) reported that "heating the testis does not damage all the cells there to the same extent. The most sensitive cells seem to be the primary spermatocytes during pachytene and the young spermatids. The later spermatids are apparently resistant,

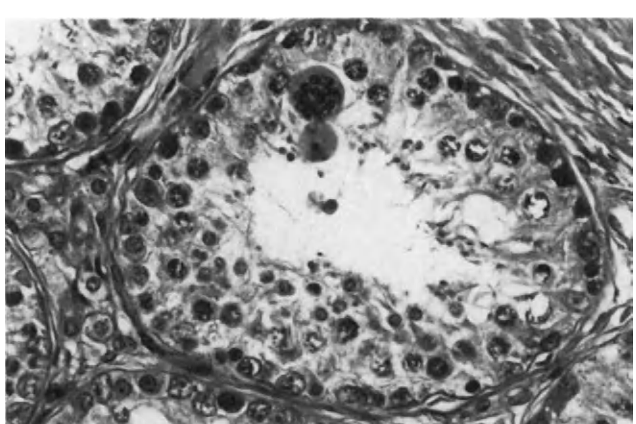

Fig. 14.6. Canine seminiferous tubule with multinucleated giant cells, individual necrotic germinal cells, and vacuoles. ×355. Acc. No. 16234.

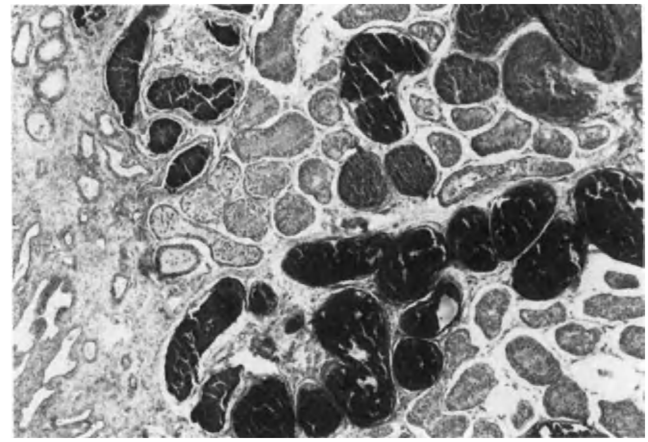

Fig. 14.7. Caprine testis with sperm stasis and mineralization of seminiferous tubules near the rete testis. ×35. Acc. No. 19283.

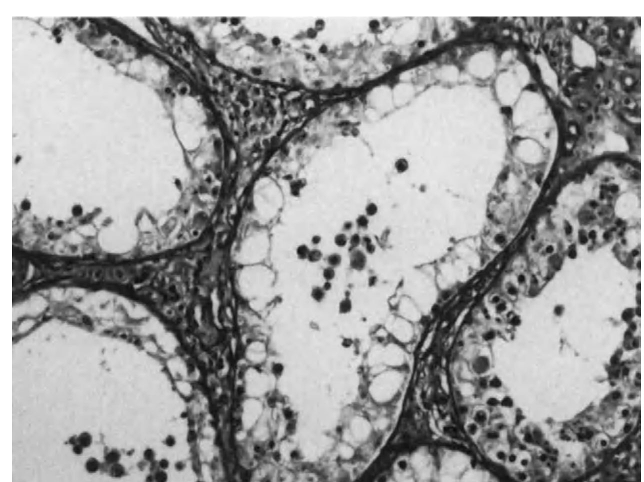

Fig. 14.8. Marked loss of germinal cells in degenerate bovine testis. Vacuolated seminiferous epithelium and sloughed germinal cells in the lumina of tubules. ×123. Acc. No. 16057.

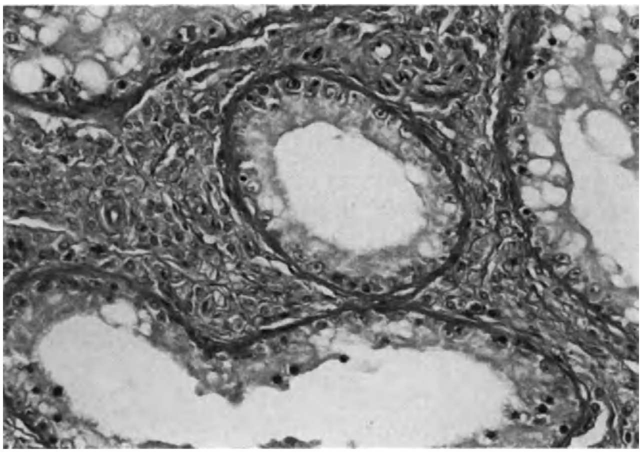

Fig. 14.9. Advanced testicular degeneration in a bovine testis. Only a few pyknotic germinal cells remain. Note the thick basement membranes. ×178. Acc. No. 5263.

and the sensitivity of the spermatogonia depends on the species." An increase in the testicular temperature causes degeneration of spermatogonia in the ram and bull, but the spermatogonia of the rat are more resistant to heat. Following restoration of physiologic temperatures, the testis recovers. However, repeated exposure to heating leads to a progressive decrease in testicular weight in rats (Bowler, 1972).

Cold. Faulkner *et al.* (1967) reported testicular degeneration associated with scrotal frostbite in bulls. They stated that "The meteorologic conditions causing scrotal frostbite were rain turning to ice and snow, accompanied by several days of temperatures lower than −25°C and winds gusting to 60 mph. Bulls provided with wind shelter, dry bedding and feed did not suffer severe scrotal frostbite. The greater incidence and severity of scrotal frostbite among older bulls may be related to their more pendulous, and thus exposed, scrotums." It was reported that bulls with poor quality semen frequently had adhesions between the scrotum and testes. "Satisfactory spermatogenic function was regained in some bulls over a period of a few months" (Faulkner *et al.*, 1967).

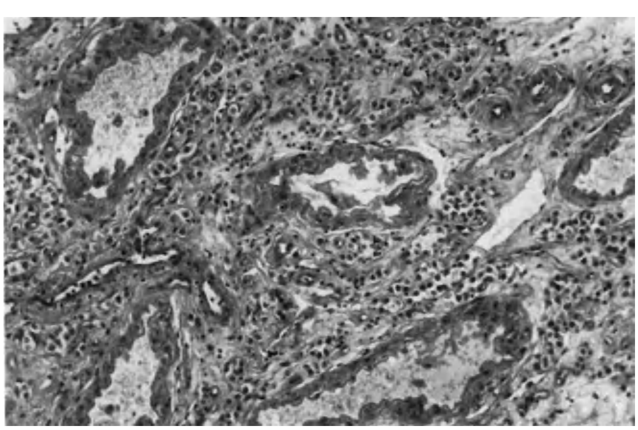

Fig. 14.10. Advanced degeneration of the testis from an 11-year-old bull. All the epithelial cells have been lost from the seminiferous tubules, which consist merely of thickened, wrinkled fibrous tissue. ×89. Acc. No. 9936.

Radiation. The type A spermatogonia are the most sensitive testicular cells to x-ray irradiation. As the dose of x-ray irradiation is increased, other germinal cells are killed in the following order: spermatids, spermatocytes, and spermatozoa. Setchell (1978) stated that "Higher doses of X-irradiation also produce chromosome damage in spermatocytes and spermatids. Mature sperm can still fertilize eggs after 65,000 R, but induced genetic abnormalities prevent the embryos from developing" (Chang *et al.*, 1957). Sustentacular cell numbers are reduced by irradiation in immature animals.

Ultrasound. Testicular degeneration has been induced in rats by exposure of the testes to high-frequency sound waves (Dumontier *et al.*, 1977).

Ischemia. Experimentally induced ischemia produces testicular degeneration in rats (Setchell, 1978).

Nutritional Disorders

Vitamin A Deficiency. Vitamin A deficiency causes testicular degeneration in the cat, bull, ram, and boar.

Vitamin A Excess. Excess vitamin A has been reported to inhibit spermatogenesis in the rat (Biswas and Deb, 1965).

Seawright *et al.* (1970) reported that hypervitaminosis A induced testicular degeneration in cats: "Testicular degeneration was apparent after 12 to 15 months on a diet of liver. . . . The testes of the affected males were soft and flabby, although secondary male characteristics had developed normally."

Deficiencies of B Vitamins. Thiamine, pyridoxine, biotin, and pantothenic acid deficiencies cause testicular degeneration in rats.

Vitamin C Deficiency. Vitamin C deficiency in guinea pigs results in degeneration of seminiferous epithelium and interstitial cells.

Vitamin E Deficiency. Vitamin E deficiency produces irreversible degeneration of the germinal epithelium in rats, guinea pigs, and hamsters but not in rabbits, mice, and domestic ruminants.

Mineral Deficiencies. Zinc deficiency induces atrophy of the testes in young rams and rats. The condition is reversible in rams but not in rats (Underwood and Somers, 1969). The effects of zinc deficiency on the testes have also been reported in cattle, goats, dogs, and mice (Miller and Miller, 1964; Miller *et al.*, 1964; Pitts *et al.*, 1966). General debility associated with many other mineral deficiencies results in testicular degeneration.

Deficiency of Energy and Protein. Deficiency of energy and protein retards development of the reproductive organs in young animals, but in adults the reproductive system continues to function unless the dietary restriction is severe (Leathem, 1975).

Amino Acid Deficiencies. It has been reported that deficiencies of arginine, leucine, lysine, tryptophane, phenylalanine, and histidine cause impairment of spermatogenesis (Setchell, 1978).

Deficiency of Fatty Acids. Testicular degeneration has been produced in rats and rabbits by feeding diets deficient in essential fatty acids (Ahluwalia *et al.*, 1967; Bieri *et al.*, 1969).

Metal Compounds. Small doses of cadmium cause necrosis of the testis (Parizek and Zahor, 1956). A few interstitial cells beneath the capsule survive and give rise to interstitial cell tumors (Gunn *et al.*, 1965).

Organic mercurial compounds, lead salts, sulfur-containing compounds, diesters of methane sulfonic acid, and monoesters of methane sulfonic acid induce testicular degeneration (Setchell, 1978).

Nitrogen-Containing Compounds. The nitrogen-containing compounds that produce testicular lesions include nitrofurans, dinitropyrroles, nitroimidazoles, quinazolinone and benzimidazole derivatives, aziridines, hydroxyurea, pipecolinomethylhydroxyindane, dimethylnitrosamine, and nitrogen mustards (Setchell, 1978).

Halogenated Compounds. The following halogenated compounds have been reported to cause testicular degeneration: bis(dichloroacetyl)diamines, thiophenes, fluoroacetamide, ethylene dibromide, hexachlorophene, and sodium 2-methyl-chlorophenoxyacetate (Setchell, 1978).

Phosphorous-Containing Compounds. Hexamethyl phosphoramide and trimethyl phosphate have been shown to induce testicular degeneration in rats (Jackson *et al.*, 1969; Jackson, 1970).

Hormones. Meinecke and McDonald (1961) found that the intramuscular injection of 250-mg doses of testosterone proprionate three times weekly for 18 weeks caused depression of semen quality and testicular size in 21- to 26-month-old Hereford bulls. The semen quality returned to normal approximately 11 weeks after cessation of testosterone injections.

Excess estrogen causes testicular degeneration in all species of domestic mammals. Dogs are more sensitive than bulls. Thus, dogs that are given estrogen and many with sustentacular cell tumors (see Chapter 15) develop advanced testicular degeneration. Bulls may be given diethylstilbestrol in 50-mg doses weekly for several years without completely inhibiting spermatogenesis.

Blind Efferent Ductules. Obstructive lesions in all the efferent ductules result in edema and degeneration of the testes. If one or both testes of a sexually mature young animal are markedly enlarged, and there are no signs of orchitis, congenital occlusion of the efferent ductules should be suspected. The failure of all the efferent ductules to join the epididymis results in the accumulation of fluid within the testis. The affected testis will be enlarged, and clear fluid will run from the cut section. Histologically, the seminiferous tubules have a large diameter but very few germinal cells (Fig. 14.11). Edema fluid is present in the interstitial tissue.

Highly Chlorinated Naphthalene. McEntee and Olafson (1953) reported that the vesicular glands, ampullae, and epididymides undergo squamous metaplasia and the testes degenerate in bulls with highly chlorinated naphthalene poisoning.

Olson and Skidmore (1954) fed pellets containing highly chlorinated naphthalene to two 3-month-old

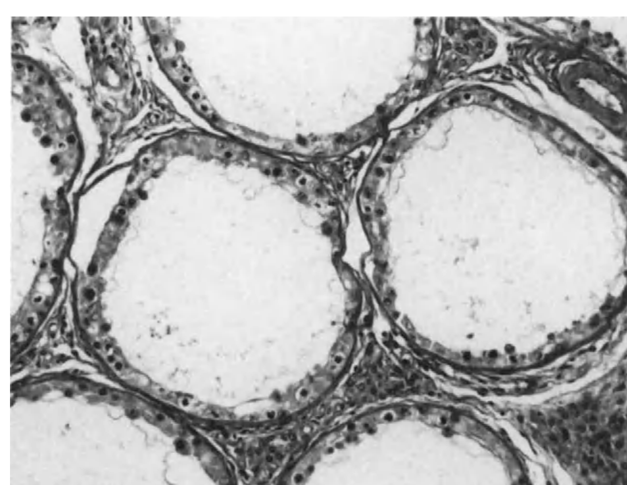

Fig. 14.11. Testicular degeneration with widely dilated seminiferous tubules from a bull with aplasia of the entire epididymis. ×125. Acc. No. 15916.

bull calves over periods of 105 and 170 days. Both calves lacrimated, failed to gain normally, and developed mild hyperkeratosis of the withers, neck, and cheeks. They recovered and were fertile at 18 months of age.

Vlahos *et al.* (1955) recorded the effects of poisoning a yearling bull with 1.8 g of penta- and hexachloronaphthalene administered over a period of 7 weeks. The blood plasma vitamin A dropped from 22.14 to 4.05 μg per 100 ml, and no motile sperm were present in the ejaculates for about 6 months. Then the concentration of sperm varied from 0 to 200 mm^3 for approximately 4 months. The semen returned to normal approximately 10 months after the highly chlorinated naphthalene was first administered. Two heifers were bred to this bull and conceived.

Poisonous Plants. James and Van Kampen (1971) reported the occurrence of testicular degeneration in rams that were fed *Astragalus lentiginosus* (locoweed) for 42 days.

Lysine seeds cause testicular degeneration in rats.

Vascular Lesions. Testicular degeneration may be associated with arteritis (especially in the stallion), degenerative vascular lesions in all species of domestic mammals, testicular biopsy, and compression and torsion of the spermatic cord.

Arteritis is a very common lesion of the spermatic cord, testicular capsule, and parenchyma of the testis in horses. It occurs in very young colts and is present in the majority of stallions of all ages. Focal areas of testicular degeneration and mononuclear cell infiltration accompany the vascular lesion (Fig. 14.12). Immature germ cells consisting of primary and secondary spermatocytes and spermatids are present in the semen of affected stallions. These primordial germ cells have degenerated by the time that they are ejaculated. Thus, they were not recognized as germinal cells until relatively recently. Swerczek (1975) reported the presence of immature germ cells in the semen of stallions. He examined the testes of one affected horse and found focal areas of testicular degeneration but did not mention vasculitis. Apparently the lesion does not cause infertility in most affected stallions, but it may be severe enough to cause focal areas of infarction of the testis (Fig. 14.13). The etiology of the disease has not been established. Perhaps it is due to the migration of *Strongylus edentatus* larvae, which is discussed on page 268.

Neoplasms. Testicular degeneration frequently accompanies neoplasms of the pituitary and hypothalamus. Steroid production by sustentacular and interstitial cell tumors causes testicular degeneration, especially in dogs.

Age-Associated Testicular Degeneration in the Bull. Humphrey and Ladds (1975b) conducted a quantitative histologic study of age-associated changes in the testes and epididymides of 80 beef bulls. The numbers of the various breeds were 14 Shorthorn, 11 Hereford, 7 Brahman, 7 Santa Gertrudis, and 41 Brahman or Santa Gertrudis crossbreeds. Some of the bulls had mild focal testicular calcification and/or fine adhesions on the tail of the epididymis. None of the bulls had major gross lesions in the reproductive organs. The bulls were divided into four groups as follows: young (9 months to 3 1/2 years), mature (3 1/2 to 7 years), old (7 to 10 years), and very old (more than 10 years). Twenty bulls were

Fig. 14.12. Focal testicular degeneration and inflammation in an equine testis. ×89. Acc. No. 18778.

Fig. 14.13. Pale oval area of infarction of an equine testis. The lesion is associated with severe arteritis. Acc. No. 4037.

allotted to each age group. It was not stated how many of each breed were in each group.

The right testis and epididymis of each bull were weighed. Tissue sections were prepared from the dorsal, middle, and ventral portion of each right testis and from the head, body, and tail of the right epididymis. "The mean testicular weights (±standard error) in the young, mature, old and very old groups were 172.2 ± 8.7, 264.4 ± 12.2, 252.0 ± 21.1 and 230.3 ± 10.3 g; and for the epididymis, 16.6 ± 0.6, 28.0 ± 1.3, 29.3 ± 1.7 and 26.5 ± 1.0 g, respectively" (Humphrey and Ladds, 1975b). The mean volumetric proportion (MVP) of tubular tissue to stromal tissue decreased by 6.8% between the young and mature groups. This is a highly significant ($P < 0.001$) difference.

According to Humphrey and Ladds (1975b), "The normal bovine testis has been regarded as a homogenous tissue, any section thus representing the organ as a whole. No significant difference between parenchymal volume in different regions was found by Amann (1962b). Our findings, however, demonstrated a significantly higher volume of parenchymal tissue in the dorsal region. A greater tubular volume and a lower collagen volume in the dorsal region of the testis appear to be normal in the bull." Progressive ventral degeneration of seminiferous tubules and interstitial fibrosis is an age-associated lesion in bulls. Humphrey and Ladds (1975b) stated that "although the relative volume of collagen was smaller at the dorsal locus than at other loci, irrespective of age, the greater difference in relative volumes of collagen between the dorsal and ventral loci in very old bulls (33%) as compared with young bulls (1.8%), suggested that progressive testicular fibrosis, especially ventrally, is a histological feature of aging."

When testicular fibrosis becomes advanced in the bull, it appears grossly as a wedge-shaped, firm, gray area in the ventral part of the testis (Fig. 14.14). Less frequently there are streaks of fibrous tissue scattered throughout the testis (Fig. 14.15). There is a sequential loss of germinal cells, sustentacular cells, and, finally, interstitial cells. Interstitial fibrous tissue increases, and the arterioles develop thick hyalin walls. Prominent foci of plasma cells appear in the fibrous tissue.

Age-Associated Testicular Degeneration in Other Species. Testicular degeneration associated with increased age occurs in other species of domestic mammals, but it is not well described in the literature.

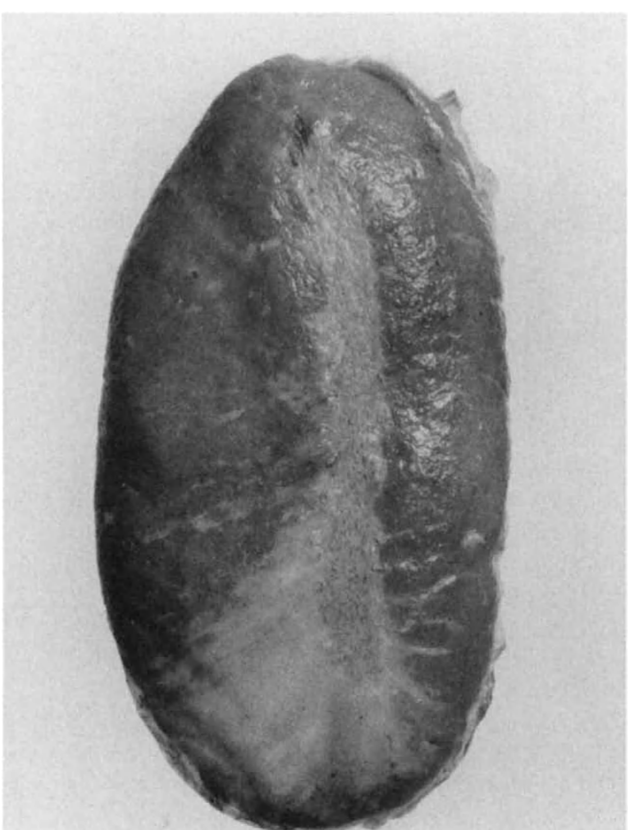

Fig. 14.14. Wedge-shaped area of fibrosis in the ventral part of the testis from a 14-year-old bull. Acc. No. 935.

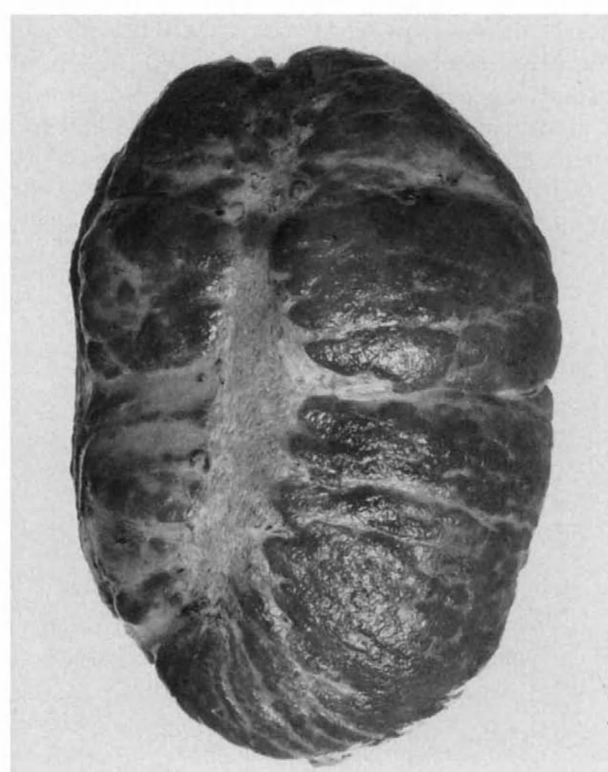

Fig. 14.15. Streaks of fibrous tissue in the testis of a 9-year-old bull. Acc. No. 845.

James and Heywood (1979) reported age-related changes in the testes and prostate of Beagle dogs but did not present a detailed description of the degenerative lesions in the testes. They mentioned that 6.3% of 48 dogs, maintained to an age of 7.75 years, had incomplete spermatogenesis and 8.3% had arterial lesions. Ten percent of this group had testicular neoplasms, and an additional 8% had interstitial cell hyperplasia. The tissues were fixed in formalin. Thus, some of the degenerative testicular lesions may have been overlooked.

I have seen ventral fibrosis in the testes of aged stallions and advanced testicular degeneration associated with arterial sclerosis in old dogs. The lesion in dogs may be diffuse or focal with areas of advanced degeneration scattered throughout the testis. Some tubules are lined merely by sustentacular cells, and others have no epithelial lining.

Testicular Calcification. Barker (1956) reported calcification of seminiferous tubules associated with testicular degeneration in bulls. Fraser and Wilson (1966) stated that "Generally, testicular calcinosis was associated with reduction in semen qualities and hence, varying degrees of infertility." They reported that the condition occurs in up to 30% of bulls, 40% of goats, and 3% of sheep. Traumatic testicular injuries usually cause focal areas of calcification that are largest in the peripheral portion of the testis, while other causes of testicular degeneration result in tubular calcification that commences adjacent to the rete testis and is scattered throughout the testis.

Traumatic Lesions. Traumatic rupture of the testis appears to be comparatively rare in domestic mammals. I have seen only two bovine cases. One bull was in a stall and apparently slipped and crushed the left testis on a water cup. The scrotum became distended with blood. The crushed testis was removed surgically 7 days following the accident. Approximately 600 ml of clotted blood surrounded the testis and spermatic cord. A 9-cm-long rupture was present in the ventral part of the testicular capsule. It extended from the midlateral part of the testis to the tail of the epididymis. The parenchyma of the entire testis was dull red and necrotic.

Smith (1940) reported a hematoma of the left testis in a 2-year-old Hereford bull that was in a corral with several other young bulls. The affected testis contained a large blood clot and weighed about 1100 g.

Traumatic injuries of the equine testis may result from a stallion being kicked by a mare during attempted service. Severe injuries cause hemorrhage, adhesions, and ventral fibrosis (Figs. 14.16 and 14.17).

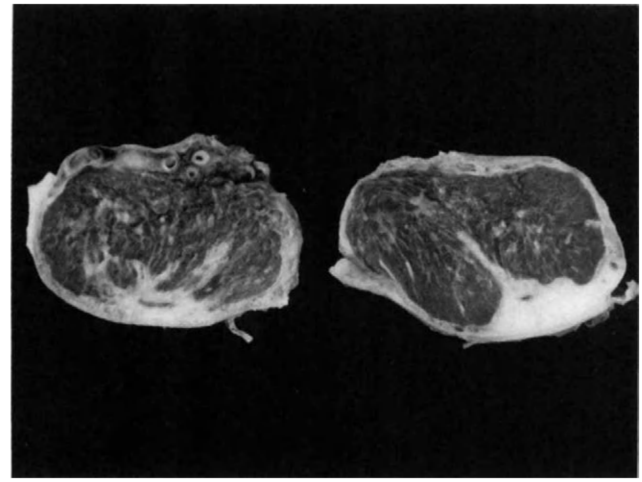

Fig. 14.16. Ventral fibrosis of the testes from a 20-year-old stallion. There were dense adhesions between the ventral portion of the testes and the parietal tunics. Acc. No. 15283.

Chapman and Williamson (1981) reported a case of massive hemorrhage in the left scrotal sac of a 3-year-old Merino ram. The scrotal content continued to increase over a period of 5 months until the scrotum was dragging on the ground. Hemicastration was performed, and an 8-kg mass of organized blood clot and an atrophic testis were removed. The ram recovered and was fertile.

Nitschke *et al.* (1976) reported testicular lesions due to trauma in 20 boars at an artificial insemination center. The testes and epididymides were enlarged, and there was a reduction in semen quality. It appeared that the testicular damage was due to skidding and falling on slippery flooring. Vascular lesions were found mostly in the ventral part of the testis and epididymis.

Orchitis and Periorchitis

Orchitis is inflammation of the testis, and periorchitis is inflammation of the tunica vaginalis testis. The lesions may occur independently or together. Bacteria are the most commonly recognized cause of these lesions, which may develop hematogenously from other parts of the body, through retrograde migration from the ductus deferens and epididymis, or directly through wounds of the scrotal skin. If orchitis is unilateral and accessory reproductive organs are not involved, the affected testis may be surgically removed and fertility will return. Temporary degeneration in the noninflamed testis is due to heat caused by inflammation of the infected testis. *Brucella*-infected animals should not be used as sires because of the possibility of spreading the disease.

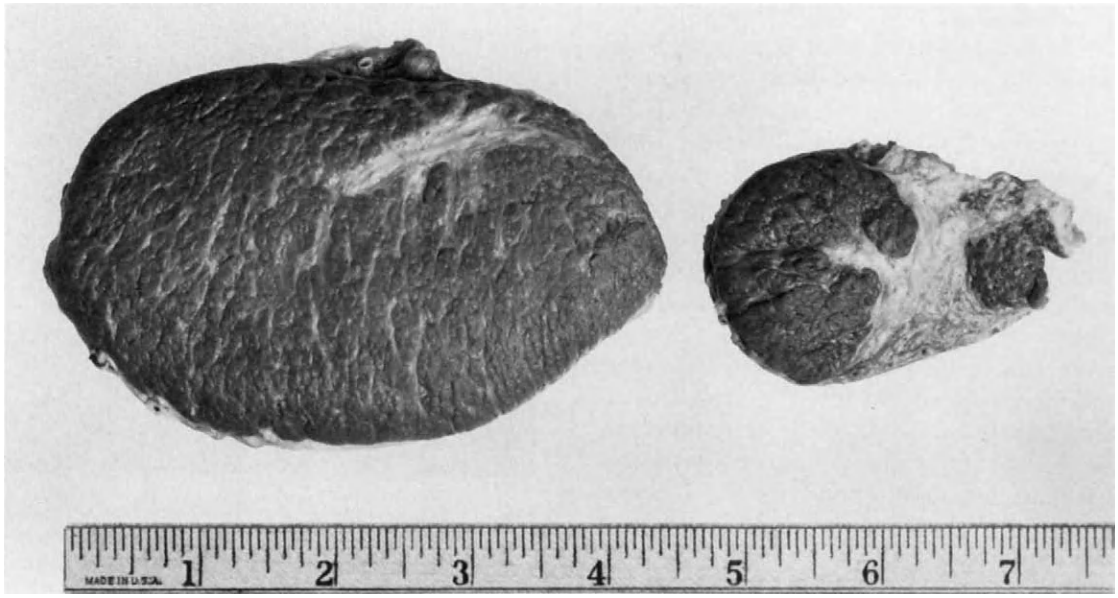

Fig. 14.17. Atrophy and fibrosis of the right testis from a 20-year-old stallion. The right testis weighed 45 g and the normal left testis weighed 251 g. Acc. No. 1063.

Bacterial Infection

Brucellosis in Cattle. The field strain and strain 19 of *Brucella abortus* are both capable of producing periorchitis and orchitis in the bull (Fig. 14.18). However, as with many bacterial infections of the male reproductive organs, the vesicular glands and the epididymides are infected more frequently than the testes. It is not unusual for orchitis to be unilateral. Plant *et al.* (1976) listed many of the references concerning *B. abortus* infection of bulls.

In suspected cases of brucellosis in the bull, the semen as well as blood serum should be tested for antibody. It is not unusual for the semen antibody level to be higher than that of the serum. In some cases the blood serum is negative, and the semen is positive (Bendixen and Blom, 1947; Christensen, 1948).

The swollen scrotum of infected bulls is hot and doughy as a result of inflammatory lesions in the testicular tunics. The cavity of the testicular tunics becomes filled with fibropurulent exudate. *Brucella* orchitis is characterized by the presence of multifocal areas of necrosis containing neutrophils. These foci are surrounded by macrophages, lymphocytes, and plasma cells (Fig. 14.19). Many of the seminiferous tubules are destroyed, and the rest undergo severe degeneration. The vascular supply to the testis may become occluded in advanced cases of periorchitis, resulting in infarction of the testis. Although *B. abortus* is mainly associated with infection of cattle, it is also found in horses, goats, sheep, dogs, and cats.

Brucella organisms can be demonstrated in smears

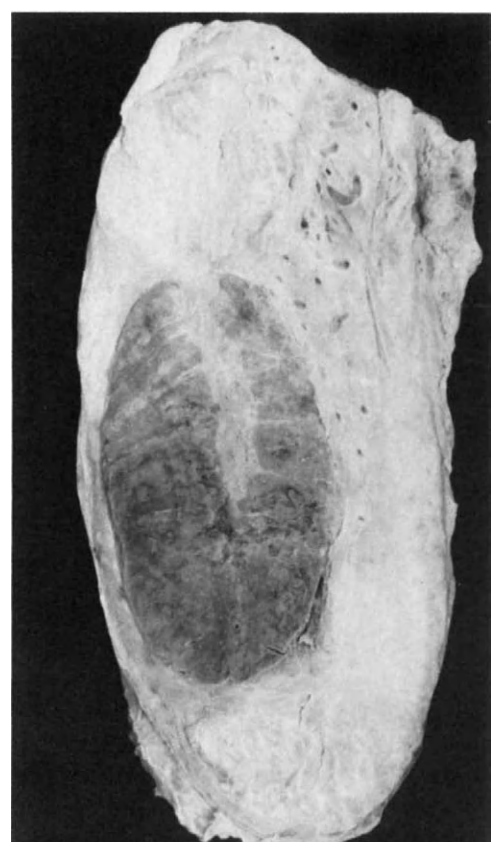

Fig. 14.18. Chronic periorchitis, orchitis, and testicular degeneration due to the field strain of *Brucella abortus* in a bull. Acc. No. 2003.

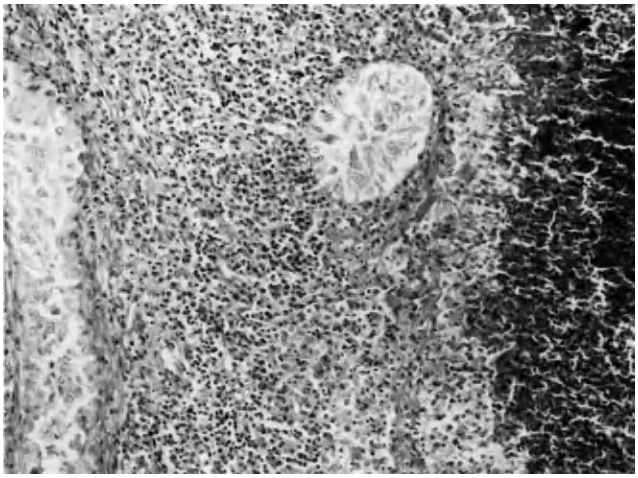

Fig. 14.19. *Brucella abortus* orchitis in a bull. ×96. Acc. No. 2003.

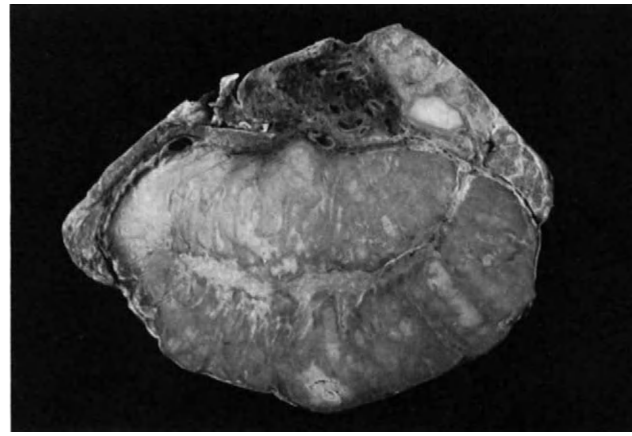

Fig. 14.20. Multifocal abscesses due to brucellosis in the testis and epididymis of a boar. Acc. No. 19617.

and tissue sections by use of the modified Ziehl–Neelson stain reported by Edgar *et al.* (1956).

Brucellosis in Swine. Brucellosis in swine is usually due to *Brucella suis,* and the infection is generally spread by sexual contact. Cattle, horses, dogs, and cats may become infected by *Brucella suis.* In a group of 11 infected boars, Thomsen (1934) reported the recovery of *B. suis* from the vesicular glands in 7 boars, epididymides in 5, testes in 2, prostate in 1, and bulbourethral gland in 1. Deyoe (1968) inoculated 14 boars with *Brucella suis* types 1 and 3 and slaughtered them 1 and 12 weeks later. Histologic lesions were found most frequently in lymph nodes, accessory reproductive organs, liver, and bone. None of the boars had testicular lesions. It appears that orchitis due to brucellosis is a secondary lesion that develops occasionally in chronic cases of infection. When present, gross testicular lesions consist of multifocal abscesses (Fig. 14.20).

The histologic lesions consist of large multifocal accumulations of neutrophils with areas of necrosis and mineralization. The surrounding tissue contains macrophages, lymphocytes, plasma cells, and fibroblasts. In advanced cases, practically all the seminiferous tubules are destroyed.

Brucellosis in Sheep. *Brucella ovis* infection of rams causes epididymitis and testicular atrophy. Adhesions develop between the testicular tunics, but orchitis does not appear to be a significant lesion in infected rams.

Brucellosis in Dogs. Infection of the canine testis can be due to *B. abortus, B. suis,* or *B. melitensus,* but most cases of orchitis are due to *B. canis.* Carmichael and Kenney (1968) reported that infected dogs frequently have scrotal dermatitis, epididymitis, and testicular atrophy that is often unilateral. The scrotal lesions occur between 1 and 2 weeks following intravenous inoculation of *B. canis* and 3 to 5 weeks after oral inoculation. Carmichael and Kenney (1970) concluded that "The scrotal dermatitis was caused principally by nonhemolytic staphylococci that had invaded the moist scrotum, probably as a consequence of persistent licking of the area over painful epididymides." They stated that "orchitis is not a salient feature of canine brucellosis" and that "rather than true orchitis, we have found more often both acute and chronic necrotizing arteritis and phlebitis."

Moore and Kakuk (1969) reported the occurrence of orchitis in *B. canis*-infected dogs. They conducted bacteriologic, serologic, and histologic studies of 18 male dogs with agglutination titers to the organism. They stated that "Of the 14 dogs with testicular abnormalities, nine had lesions in both testicles. Degeneration of seminiferous tubules was sometimes the only abnormality observed. Some degenerating seminiferous tubules contained only spermatogonial and Sertoli's cells; lymphocytes, histiocytes and cells of reticular origin were found throughout the interstitial layer. Extensive testicular involvement resulted in almost total loss of seminiferous tubules and replacement by fibrous tissue interspersed with lymphocytes" (Fig. 14.21). Gleiser *et al.* (1971) also reported chronic orchitis and degeneration of the seminiferous epithelium in dogs with *B. canis* infection.

Unilateral testicular necrosis has been reported in association with canine brucellosis (Schoeb and Morton, 1978). *Brucella canis* was isolated from draining ulcers in the scrotum. "The right testicle was normal, but the entire left testis was necrotic, being composed of soft, yellow-green, friable caseous material. The

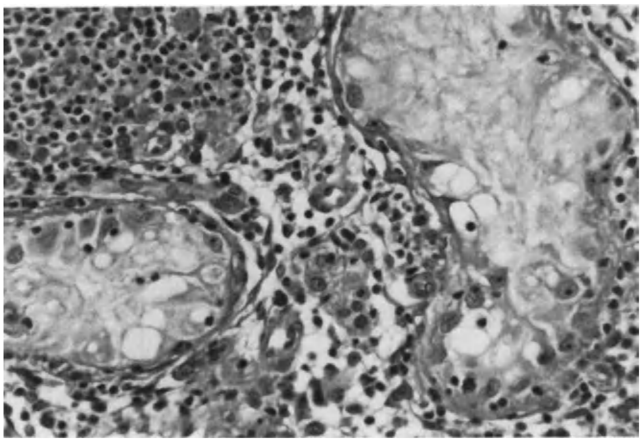

Fig. 14.21. Canine orchitis due to *Brucella canis*. Acc. No. 11932.

cavity of the tunica vaginalis was obliterated by tough fibrous adhesions between the common and proper tunics" (Schoeb and Morton, 1978). Although the cause of the testicular necrosis was not determined, it is possible that infarction occurred as a consequence of arteritis.

Tuberculosis. Tuberculous orchitis occurs rarely in cattle and swine, and as with most genital infections, the testis is affected less frequently than the epididymis. Jubb and Kennedy (1963) stated that "Involvement of the testis may take one of two anatomical forms, being either miliary tuberculosis or chronic testicular tuberculosis. In the former, small or large caseous and calcified foci are irregularly scattered throughout the testes but may spare the epididymis entirely. In chronic testicular tuberculosis, the cut surface of the enlarged testis reveals broad bands of caseous necrosis radiating out from the rete testis, and the epididymis is usually involved."

Glanders. Glanders is one of the oldest known diseases of horses and was recognized as contagious as early as the 17th century. According to Schlegel (1924), suppurative malleous orchitis occurs rarely in horses and arises following the hematogenous spread of *Actinobacillus (Malleomyces) mallei*. It appears as multifocal or diffuse areas of caseation or suppuration of the testis. Soft foci of creamy or caseous material are present in the glandular substance and are surrounded by proliferating connective tissue.

Pseudomonas pseudomallei Infection. Joseph *et al.* (1974) reported that *Pseudomonas pseudomallei* is a common cause of porcine orchitis in Malaysia. They recorded a case in which one infected testis weighted 4.3 kg and "the majority of the space within the tunics was taken up by a large mass of thick, creamy, greenish-yellow pus." The prostate and vesicular glands contained purulent exudate. Abscesses were present in the liver and lungs. *Pseudomonas pseudomallei* was isolated from the testes, prostate, lymph nodes, kidney, and lung. "Microscopically, the main lesions consisted of localized areas of caseation necrosis, infiltrated by large numbers of mononuclear cells. These necrotic areas were encapsulated by a thick layer of fibrous tissue, within which variable numbers of lymphocytes and plasma cells were scattered" (Joseph *et al.*, 1974). The inflammatory nodules were present in many organs but were not numerous in the lungs and testes.

Haemophilus somnus Infection. Metz *et al.* (1984) reported a case of chronic orchitis and epididymitis in a 3-week-old calf. The right testis was enlarged, and the left testis was undescended. The enlarged testis was replaced by a thick-walled abscess and measured about 8 by 4 cm. Multifocal abscesses were present in the epididymis and spermatic cord, and *Haemophilus somnus* was isolated from the exudate.

Actinomyces bovis Infection. Kimball *et al.* (1954) reported the isolation of *Actinomyces bovis* from six cases of orchitis in bulls. Ayers *et al.* (1977) recorded a case of actinomycosis of the spermatic cords, epididymides, and testes in a dog.

Corynebacterium pseudotuberculosis Infection. Caseous lymphadenitis causes abscesses in the scrotal fascia of sheep. Williamson and Nairn (1980) stated that "semen quality was normal in all rams affected with abscesses caused by *C. pseudotuberculosis* in the scrotal fascia, even those with lesions up to eight cm long and six cm diameter." They emphasized the importance of distinguishing "between lesions caused by *C. pseudotuberculosis* and other palpable lesions of the scrotum of rams, as epididymitis, spermatoceles and varicocoeles."

Miscellaneous Bacterial Infections. Orchitis, due to a variety of bacterial infections, occurs occasionally in all species of domestic mammals. Bulls may develop orchitis and/or periorchitis as a result of infection by *Actinomyces pyogenes (Corynebacterium pyogenes)* (Fig. 14.22), *Escherichia coli*, *Hemophilus* spp., *Salmonella* spp., *Actinomyces bovis*, *Norcardia farcinica*, streptococci, or staphylococci. Some of the organisms isolated from cases of orchitis in boars include *Actinomyces pyogenes*, *Streptococcus equisimilis*, *Streptococcus zooepidemicus*, and *Pseudomonas pseudomallei*. Testicular abscesses in the ram may be due to infection with *Actinomyces pyogenes* and *Corynebacterium pseudotuberculosis*.

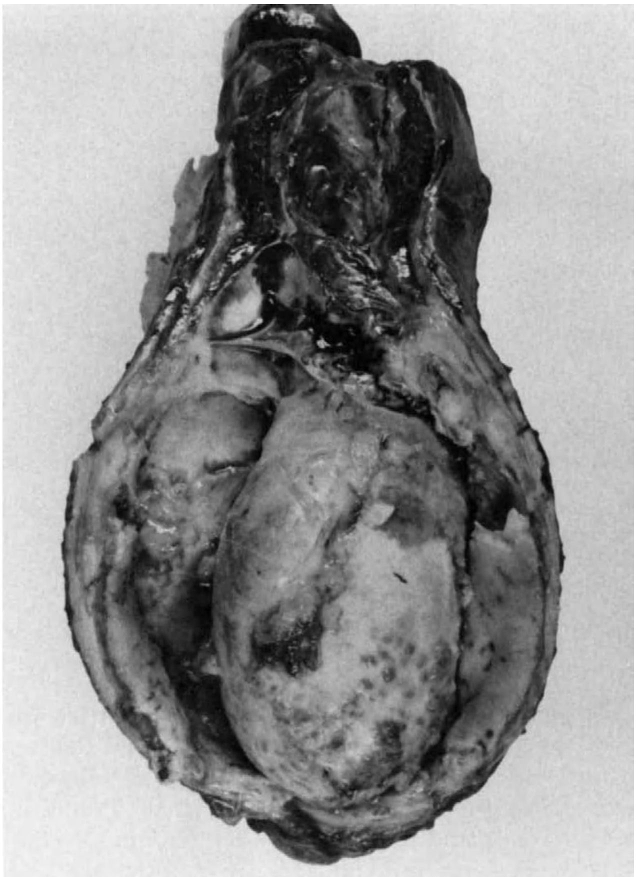

Fig. 14.22. Periorchitis due to *Actinomyces pyogenes* in a bull. Acc. No. 2100.

Salmonella abortus equi causes testicular abscesses in the stallion. *Escherichia coli* and *Proteus vulgaris* cause orchitis in dogs.

Mycoplasmal Infection. McIlwain and Bolin (1967) reported that a *Mycoplasma* was isolated from the testes of three rams with greatly enlarged gonads: "Histologic examination revealed small necrotic areas throughout the tissue cuffed by mixed inflammatory exudate. The predominant cells were polymorphonuclear leukocytes, although occasional mononuclear cells were seen."

Chlamydial Infection. Chlamydiae have been isolated from the testes of bulls with granulomatous orchitis. However, the naturally occurring disease has not been reproduced by either intramuscular or intratesticular inoculation of various strains of this organism. Furthermore, the intratesticular injection of chlamydiae does not always produce an inflammatory response. Jaskowksi and Sadowski (1980) concluded that "these facts raise doubts as to the primary character of the chlamydial agent as the cause of chronic granulomatous orchitis in bulls."

Viral Infection

Bovine Enterovirus Infection. Bouters (1964) and Bouters and Vandeplassche (1964) reported the occurrence of testicular degeneration in bulls that were experimentally infected with an enterovirus. The semen quality returned to normal within 2 to 3 months following infection.

Equine Infectious Anemia. The equine infectious anemia virus causes multifocal areas of necrosis in the testes of some stallions.

Canine Distemper. Intranuclear and cytoplasmic inclusion bodies occur in the sustentacular cells of the testis in cases of canine distemper (Fig. 14.23). The inclusions are usually found in the seminiferous tubules adjacent to the rete testis. The virus causes testicular degeneration in sexually mature dogs.

Protozoal Infection. Dourine, due to *Trypanosoma equiperdum*, is usually spread from stallion to mare and vice versa during coitus. The trypanosomes may be present in the seminal fluid and mucus exudate of the penis and sheath of the stallion and in the vaginal mucus of the mare. The external genital lesions in the stallion consist of edematous plaques on the penis and prepuce. The connective tissue of the spermatic cord often contains a yellow gelatinous infiltrate. Mohler and Schoening (1935) reported that "The tes-

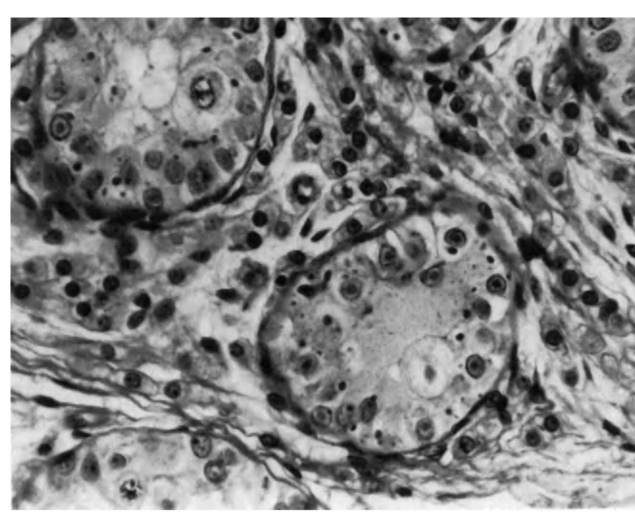

Fig. 14.23. Intranuclear and cytoplasmic inclusions in the sustentacular cells of the testis in a sexually immature dog with distemper. ×374. Acc. No. 10456.

ticles in some cases are soft and smaller than normal, while in others the opposite is found. Adhesions may be found between the different coverings of the testicles." The testes may contain caseous inflammatory foci. Abscess formation and sloughing occurs in some cases.

Ikede (1979) reported that "Rams inoculated intravenously with *Trypanosoma brucei* developed scrotal oedema and a nonsuppurative granulomatous periorchitis resulting in testicular degeneration, atrophy, calcification and sclerosis. The tunica vaginalis was the seat of an intense granulomatous inflammation and focal necrosis, which extended to the epididymis and spermatic cord. . . . In areas where there was inflammation or focal necrosis, there was also extravascular localization of trypanosomes."

Parasitic Lesions

Strongylus edentatus. Hobday (1922–1923) reported that *Strongylus edentatus* is found frequently in the testicular tunics or within the testis of cryptorchid horses.

Smith (1973) found *Strongylus* larvae in the testes of 11 pony stallions ranging in age from 2 to 7 years. One was a bilateral cryptorchid with larvae in both testes. "The remaining ten ponies had only one affected testicle, seven were abdominal, two were inguinal and one was a hypoplastic testicle." Larvae and their tracks were found in the spermatic cord and in the testis anywhere from just below the tunica albuginae into the center of the gonad. The parasitic tracts were surrounded by red blood cells and leukocytes, many of which were eosinophiles. All the larvae were identified as *Strongylus edentatus.* "The specimens recorded in this study represent aberrant fifth-stage larvae which have passed into the mesorchium, which arises from the dorsal abdominal wall close to the mesocolon and have migrated down the spermatic cord. . . .The migration occurs under the peritoneum covering the spermatic cord, and the spermatic artery is not involved" (Smith, 1973).

I have seen a number of narrow, elongated, granulomatous lesions induced by migrating strongyle larvae on the surface of descended equine testes. However, I have not seen a case of invasion of the testicular parenchyma by larvae in normally descended testes. The only cases involving testicular invasion have occurred in cryptorchid testes (Fig. 14.24). Squamous metaplasia occurs in the appendix testis (Fig. 14.25) when it is invaded by strongyle larvae. This lesion should not be confused with a squamous cell carcinoma.

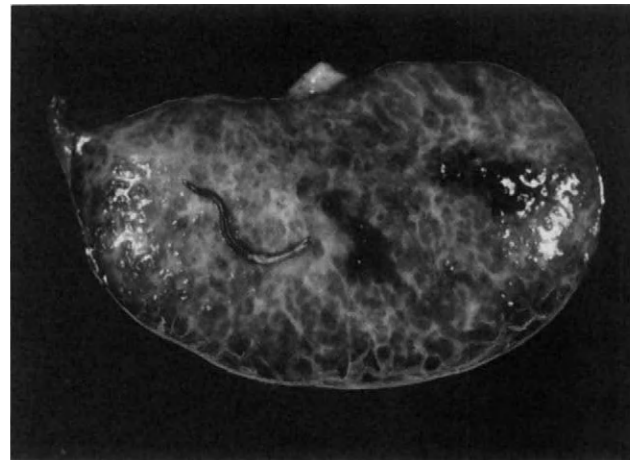

Fig. 14.24. Hemorrhagic tracts caused by migration of a *Strongylus edentatus* larva in an abdominal testis of a 4-year-old horse. A portion of the larva is on the surface of the incised testis. Acc. No. 18335.

Setaria labiatopapillosa. Powe and Powers (1985) reported that eight bulls with granulomatous periorchitis were seen at the Auburn University Large Animal Clinic. Histologic examination revealed that the lesions were due to a helminth that they assumed was *Setaria labiatopapillosa.* They stated that "Practicing veterinarians and the authors have seen periorchitis develop in some bulls one to two months after the injection of tetramisole. One producer had eight bulls in which periorchitis developed within one month after deworming with injectable tetramisole."

Focal granulomatous lesions occurred in the tunica vaginalis of bulls following implantations of dead nematodes *(Setaria labiatopapillosa)* into the vaginal

Fig. 14.25. Squamous metaplasia of an equine appendix testis due to invasion by strongyle larvae. ×51. Acc. No. 18915.

cavity of the testis. The lesions were similar to those in some clinical cases of periorchitis. Similar lesions also developed when live worms were placed in the vaginal cavity, and the bulls were treated with tetramisole 6 days after implantation.

Mesocestoides spp. Barsanti *et al.* (1979) reported a case in a dog of peritonitis and periorchitis due to infection by cestode larvae of the presumptive genus *Mesocestoides.*

Cuterebra emasculator. *Cuterebra emasculator* was misnamed because it was originally thought that the warbles emasculated squirrels. Sabrosky (1986) stated that "The inguinal region is apparently the usual location for larvae of *emasculator,* which has aided and abetted the story. However, recent authorities have concluded that the situation was misinterpreted, that the testes are normally withdrawn into the abdomen in the season when bot larvae are commonly present, and therefore, hunters assumed that the animals had been castrated by the larvae. . . . Recent authors have critically studied the problem and have found no evidence of emasculation, either in nature or in experimental studies." Bloom (1954) reported that the larvae occasionally invade the scrotum of the dog.

Onchocera ochengi. Akusu *et al.* (1983) diagnosed a case of scrotal onchocerciasis in a bull in Nigeria. A firm, 2.5-cm, white, lobulated nodule was present in the neck of the scrotum. "Numerous worms were observed microscopically in three worm nests in the deeper regions of the dermis. The worms were mostly adult females containing large numbers of embryonated eggs and microfilariae in their uteri" (Akusu *et al.,* 1983). They concluded that the parasite was *Onchocera ochengi* because of its location in the scrotum and the small size of the microfilariae (mean length 153.2 ± 35.2 μm).

Focal Lymphocytic Orchitis in the Stallion. Focal areas of lymphocytic infiltration of the testis associated with arteritis and focal degeneration of seminiferous tubules is an extremely common lesion in horses. In fact, very few stallions are free of lesion. The vascular lesions are most severe in the testicular tunic and may extend into the spermatic cord. Multifocal areas of necrosis have been seen in a few severely affected testes. Although numerous primordial germ cells, from the focal areas of testicular degeneration, may be present in the semen, fertility is not usually affected. The etiology of the lesions has not been determined. Possibly migrating larvae of *Strongylus edentatus* may be involved.

Noninfectious Multifocal Orchitis. Small perivascular and peritubular foci of lymphocytes occur frequently around areas of testicular degeneration. This appears to be an inflammatory reaction associated with autoimmunity, but the etiology has not been determined.

Peritubular granulomatous lesions sometimes surround seminiferous tubules with sperm stasis. This lesion is seen most frequently in the bull.

Allergic Epididymo-Orchitis. Young, sexually mature guinea pigs are especially prone to develop allergic epididymo-orchitis when they are isoimmunized with testicular material. Thus, they have been the animal of choice for most of the experimental studies of the condition. Johnson (1970) and Tung *et al.* (1970) reported inflammatory lesions in the rete testis and the efferent ductules. The condition is usually referred to as orchitis because, when the condition was first studied, the gonads were not examined histologically in the early stages of the disease. By the time they were examined, the severe inflammatory lesions in the rete testis and efferent ductules had subsided.

Parsonson *et al.* (1971) isoimmunized guinea pigs with "ammonium-sulphate-precipitated testicular material (ASPM) in Freund's complete adjuvant and killed them five, ten, 15, 20 or 60 days later." Acute inflammatory lesions occurred between 5 and 10 days in the rete testis and efferent ductules. These lesions were soon followed by marked orchitis and acute testicular degeneration. Signs of renewed testicular function were evident by 60 days, but many of seminiferous tubules were still lined predominantly by sustentacular cells.

Parsonson isoimmunized bulls once or more with

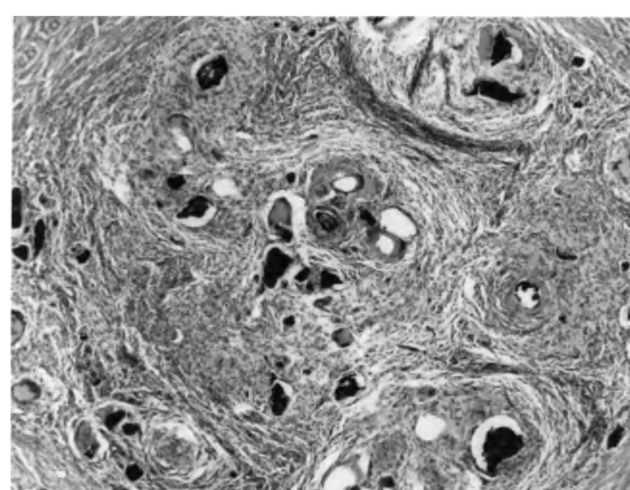

Fig. 14.26. Granulomatous orchitis in bovine testis. ×52. Acc. No. 18220.

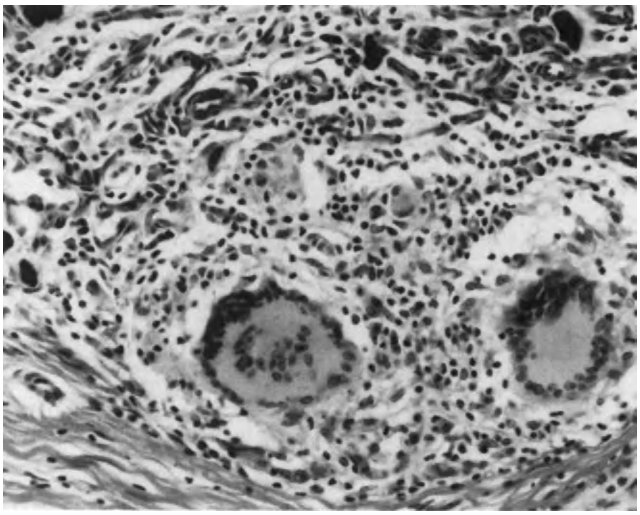

Fig. 14.27. Granulomatous orchitis in bovine testis. ×204. Acc. No. 18220.

ASPM or testicular homogenate in complete adjuvant and killed them 10 to 70 days later. Bulls killed at Day 10 had nonsuppurative inflammation in the efferent ductules and head of the epididymis and suppurative inflammation of the ampullae. There was marked edema in the rete testis and efferent ductules. Testicular degeneration was less severe than that in guinea pigs. Not all the bulls killed at later times had lesions in the reproductive organs. The occurrence of lesions following immunization was influenced by age, breed, and type of antigen used. One-year-old bulls and Guernseys were more susceptible than older animals and Holstein-Friesians. ASPM was less effective than testicular homogenate in producing allergic epididymo-orchitis.

Granulomatous Orchitis of Undetermined Etiology. Multifocal granulomatous orchitis of undetermined etiology has been seen in Europe and South America. It usually affects sexually mature young bulls. The seminiferous tubules are destroyed and the granulomas contain large multinucleated giant cells (Figs. 14.26 and 14.27). I saw the specimen from which these photos were prepared at the Rubino Institute in Uruguay.

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Chapter 15

Scrotum, Spermatic Cord, and Testis: Proliferative Lesions

Testicular Hypertrophy

Scrotal Hyperplasia

Testicular Hyperplasia

Scrotal Neoplasms

Neoplasms of the Spermatic Cord

Testicular Neoplasms
- **Interstitial Cell Tumor (Leydig Cell Tumor)**
- **Seminoma (Germinal Cell Tumor, Spermatogonioma)**
- **Sustentacular Cell Tumor (Tubular Adenoma and Adenocarcinoma, Sertoli Cell Tumor)**
- **Mixed Germ Cell–Sex Cord–Stromal Neoplasm (Gonadoblastoma)**
- **Rete Testis Adenoma and Adenocarcinoma**
- **Embryonal Carcinoma**
- **Adrenal Rest Tumors of the Testis**
- **Secondary Carcinoma of the Testis**
- **Teratoma**
- **Malignant Lymphoma**
- **Mesothelioma**
- **Tumors of the Appendix Testis**
- **Hemangioma**
- **Leiomyoma**
- **Mast Cell Tumor (Mastocytoma)**
- **Schwannoma**

Bibliography

Testicular Hypertrophy

Hypertrophy refers to an increase in the size of individual cells, but the term is often used to denote enlargement, other than neoplasia, of an organ or part when it is not known whether the enlargement is due to an increase in size or number of individual cells or both.

Voglmayr and Mattner (1968) reported compensatory hypertrophy in the remaining testis following unilateral orchidectomy in the adult ram. Nine 3- to 5-year-old rams were used. "By 120 days after hemicastration, the weight of the remaining testis had increased by 76% (SE ± 3.6%) above the weight of the testis removed at hemicastration, and by 94% (SE ± 16.7%) above the mean testis weight in the entire control animals. . . . The mean diameter of the seminiferous tubules in the hemicastrates was significantly greater than in the entire animals and had increased from 181 ± 6.5 μ at hemicastration, to 238 ± 5.9 μ 120 days postoperatively . . . [and] the expansion of the seminiferous tubules could account almost entirely for the increase in the testis weight" (Voglmayr and Mattner, 1968).

Johnson (1978) studied the effects of hemicastration on bulls at two different stages of testicular development. "Bulls were unilaterally castrated at average ages of either 928 ± 8.6 or 224 ± 3.8 days and complete castration was performed 135 and 165 days later for the two age groups, respectively. The remaining right testes of hemicastrated bulls were heavier ($P < .01$) than right testes of control bulls in both age groups at the conclusion of their experimental periods . . . the numbers of spermatogonia, pachytene spermatocytes and spermatids in Stage VII tubules and the mean diameter of seminiferous tubules was significantly greater in hemicastrated bulls as compared to control bulls."

Scrotal Hyperplasia

Bloom (1954) described scrotal hyperplasia of old dogs. He stated that "Grossly, the size of the scrotum is increased, and the scrotal skin and underlying tissue are thickened either diffusely or in the most dependent portions. The thickened areas are, as a rule, wrinkled, deeply pigmented, and hairless. Microscopically, the epithelium is markedly hyperplastic and often shows hyperkeratosis, and the subepithelial tissue shows diffuse hyperplasia of coarse fibrous connective tissue."

Testicular Hyperplasia

Hyperplasia refers to an increase in the number of cells, excluding tumor formation, whereby the entire organ or affected part of the organ increases in size. It is often difficult to draw a sharp line of distinction between hyperplasia and neoplasia. This is especially so in regard to proliferative nodules of interstitial cells of the canine and bovine testes. The distinction between focal hyperplasia and neoplasia is often arbitrary. Cotchin (1960a) stated that "An arbitrary and possibly meaningless lower limit of size of 1 cm was taken as distinguishing between ICT (interstitial cell tumors) and hyperplasia of Leydig cells; generally, at about this size, a capsule was present, or forming, around the interstitial cell mass." Innes (1942) considered all focal proliferative growths of interstitial cells, except those that had metastasized, to be nodular hyperplasia. It appears that we cannot reliably distinguish between nodular hyperplasia and neoplasia of testicular interstitial cells. Thus I arbitrarily consider all grossly visible nodules of interstitial cells in the testes of domestic mammals to be interstitial cell tumors.

I have seen a few cases of sustentacular cell hyperplasia in canine testes. The dogs were old, and some had clinical signs of feminization. Many of the seminiferous tubules were filled with sustentacular cells, but none had penetrated the basement membrane of the tubules, which were of approximately normal size (Fig. 15.1).

Hyperplasia of sustentacular cells occurs occasionally in cattle in association with testicular hypoplasia and with degeneration of the testes.

Nistal *et al.* (1982) reported hyperplasia of the sustentacular cells in the human testis. They stated that "Testicular biopsy specimens from adult patients affected with cryptorchidism, Klinefelter's syndrome, and Del Castillo's syndrome were examined by light and electron microscopy. The study revealed a high proportion of testes showing seminiferous tubules with hyperplasia of Sertoli cells (from 25 to 45 cells per transverse tubular section). These cells had an immature appearance and showed a pseudostratified distribution."

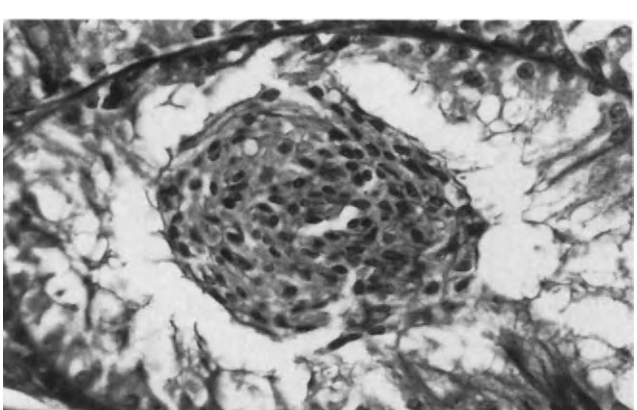

Fig. 15.1. Seminiferous tubule with hyperplasia of sustentacular cells from a 12-year-old dog. ×222. Acc. No. 18144.

Scrotal Neoplasms

There are very few reports in the literature concerning scrotal neoplasms in domestic mammals. The mast cell tumor, first described by Bloom (1942), is the most common scrotal neoplasm in the dog. I reviewed the pathology reports from the New York State Veterinary College concerning a sequential series of scrotal neoplasms in 100 dogs. Mast cell tumors (mastocytomas) were diagnosed in 88 dogs and 47 of the neoplasms were considered to be malignant. Postsurgical information was available on relatively few of the cases so the accuracy of diagnosis of malignancy is not known. A significantly high incidence, 30/88 (34%), of these scrotal tumors was found in Boxers. Seven Boston Terriers and seven Dachshunds had scrotal mast cell tumors. The other scrotal neoplasms in the dog included five hemangiomas, three melanomas, three histiocytomas, and one neurofibroma. Milks (1939) reported a fibroma of the scrotum of a cat.

Nielsen and Cole (1958) reported 100 cases of mast cell tumors in dogs. These tumors were present in the scrotum in 11 of 48 male dogs. Six of the 11 neoplasms were apparently malignant because they appeared to be immature, had many mitotic figures, recurred or had metastasized to the inguinal lymph nodes.

Patnaik *et al.* (1984) reported the morphologic grading and survival time of 83 dogs with cutaneous mast cell tumors. The neoplasms were found in 40 females and 43 males, but the location of the tumors was not mentioned. They classified the tumors into Grades I, II, and III according to increasing malignancy. They reported that "After a 1500-day follow-up period, it was observed that 93% (28/30) of the dogs with Grade I mast cell tumors had survived, while only 44% (16/30) and 6% (1/17) of those with grades II and III mast cell tumors, respectively, were still alive."

Jackson (1936) stated that the scrotum is a typical site for the canine transmissible venereal tumor. Feldman (1932) reported a fibrosarcoma in the canine scrotum and a melanoblastoma in the scrotum of a horse. Barron (1949) described an adenocarcinoma of sweat gland origin in the scrotum of a 4-year-old English Bulldog and a squamous cell carcinoma of the scrotum in a 4-year-old mongrel dog.

Weipers and Jarrett (1954) reported hemangiomatosis of the canine scrotum. They stated that "The lesions are usually seen in dogs past middle age and are particularly common in breeds with pigmented skin, such as Scotch Terriers, Airedales, Kerry Blues and Labradors." They concluded that the vascular lesions of the canine scrotum "are probably better regarded as hamartomas or growth anomalies, rather than true neoplasms. . . . This condition, in our experience, is strictly limited to the skin of the scrotum. No spread to contiguous skin has been observed either before or after surgical treatment. In every case where the whole scrotum has been removed no further trouble occurred."

Vascular scrotal lesions, similar to those of the dog, occur in the ventral portion of the scrotum of mature and aged bulls. The lesions remain localized and are considered to be malformations.

Szczech *et al.* (1973) described a hamangioma of the scrotum in a Chester White boar and referred to three other reports concerning vascular tumors of the scrotum in swine. They stated that "The neoplastic nature of the growth . . . is suggested by the age of onset, local recurrence, and spread to other areas as well as by the histopathological features. These features also suggest the possibility that the neoplasm may be malignant. Others have considered apparently similar lesions in boars to be vascular malformations."

Munro *et al.* (1982) discussed vascular lesions of the scrotum in Hong Kong and Fiji pigs. They reported that the prevalence of the condition in one herd with 30 large white boars over 2 years of age was 100%. "Initially, these vascular abnormalities appeared as tiny, purplish, slightly raised "blebs" on the skin. . . . They usually developed into warty lesions of various sizes, some of which appeared pedunculated. Some boars had only a few lesions, but others had more than 100 separate growths. In all cases, the neoplasms were confined to the scrotum and perineum" (Munro *et al.*, 1982). They commented that the vascular lesions did not appear to be neoplastic on the basis of histologic examination. However, they concluded that "Until such time as the development of these growths in pigs has been studied and a classification proposed on the basis of these findings, it would be less confusing to adhere to the term hemangioma."

Neoplasms of the Spermatic Cord

The spermatic cord and epididymis from animals with testicular tumors should be examined grossly and microscopically for the presence of primary and metastatic neoplasms. It is frequently difficult to determine the malignancy of a testicular neoplasm by merely examining a section of the tumor. Small metastatic neoplasms and small primary neoplasms of the cord will be overlooked if the tissue is not examined microscopically. Large neoplasms of the spermatic cord may cause infarction of the testis.

Primary neoplasms of the spermatic cord in domestic mammals occur predominantly in dogs, but they are rare. I have seen malignant neoplasms of adipose tissue, fibrous tissue, and striated muscle in the canine spermatic cord. Metastases of neoplasms of the spermatic cord occur first to the regional lymph nodes.

Banowsky and Schultz (1970) reviewed the literature on sarcomas of the spermatic cord and testicular tunics in man. Fibrosarcomas were diagnosed most frequently. They also reported liposarcomas, myxosarcomas, myosarcomas, rhabdomyosarcomas, leiomyosarcomas, fibromyxosarcomas, lymphosarcomas, and a few other types of connective tissue neoplasms.

Testicular Neoplasms

The most common testicular neoplasms in domestic mammals are seminomas (germinal cell tumor, spermatogonioma), sustentacular cell tumors (tubular adenoma, tubular adenocarcinoma, Sertoli cell tumor), and interstitial cell tumors (Leydig cell tumor). Testicular neoplasms occur most frequently in the dog and rarely in the cat.

I have examined 749 testicular tumors from domestic mammals, including 1 feline, 5 ovine, 30 equine, 76 bovine, and 640 canine neoplasms. I have not seen caprine or porcine testicular neoplasms.

The canine neoplasms in my collection consist of 235 seminomas, 223 sustentacular cell tumors, 175 interstitial cell tumors, and 7 miscellaneous neoplasms. Most of the neoplasms were surgical specimens. Thus the incidence of interstitial cell tumors is lower than it would have been in postmortem specimens because many of the tumors are not large enough to draw clinical attention to their presence.

The relatively large series of testicular neoplasms in bulls was found because I routinely examined the testes of all bulls, from a large artificial insemination (A.I.) center, that died of disease or were slaughtered for a variety of reasons over a period of 31 years. There were 1064 bulls of which 823 were 5 years of age and older. Most of 43 bulls that had interstitial cell tumors were over 5 years of age. Forty of the bulls were from the one stud and three were from other sources.

Sustentacular cell tumors were present in 20 bulls from the same A.I. center. Two of the affected bulls were under 2 years of age and the rest were over 5 years old. Five bulls with sustentacular cell tumors were from other sources.

Three bulls had mesotheliomas of the testicular tunics and one bull had a testicular lymphoma.

The equine testicular neoplasms consisted of 11 teratomas, 9 interstitial cell tumors, 7 seminomas, 2 lipomas, and 1 mast cell tumor. Testicular teratomas occur predominantly in young cryptorchid stallions and are extremely rare or nonreported in other species of domestic mammals.

I have seen neoplasms of the rete testis in the dog, bull, and stallion. Other neoplasms that occur occasionally in the testicular tunic and spermatic cord of domestic mammals include benign and malignant neoplasms of blood vessels, nerves, and fibrous tissue.

Dow (1962) examined the testes from 580 unselected adult dogs that were submitted for necropsy at the Veterinary School of the University of Glasgow. The testes were cut into a number of transverse sections, and tissue from both testes was examined grossly and microscopically in all cases. The internal iliac and sublumbar lymph nodes were examined for metastases. Apparently the spermatic cord and epididymis were not examined routinely for microscopic lesions. Testicular tumors were found in 94 (16%) of the 580 dogs. All the neoplasms were reported to be of sustentacular cell, interstitial cell, or spermatogonial origin. Thirty-nine (41.5%) of the dogs had more than one type of testicular tumor.

Cryptorchidism is a contributing factor to the development of testicular neoplasms. Hayes and Pendergrass (1976) reported that "Cryptorchid dogs appear to have a 13.6 times higher risk of testicular tumor than normal dogs. Additionally, male dogs with an inguinal hernia have an increased risk (4.7) of testis tumors."

Interstitial Cell Tumor (Leydig Cell Tumor)

Different opinions have been expressed concerning whether focal proliferations of testicular interstitial cells are hyperplastic or neoplastic lesions. The question has not been resolved. Arbitrary decisions concerning interstitial cell nodules in the canine testis have ranged from considering all interstitial cell nodules, except those that metastasize, as hyperplastic lesions, to diagnosing all grossly visible nodules as tumors, to calling nodules neoplastic if they are 1 cm or larger in diameter (Innes, 1942; Scully and Coffin, 1952; Cotchin, 1960a). Most focal proliferative growths of interstitial cells in other species of domestic animals have been reported as neoplasms.

Warren and Olshausen (1943) reported interstitial cell growths of the human testis. They stated that "The differentiation between hyperplasia and neoplasia in respect to certain rare tumors such as those of interstitial cells is difficult chiefly because of lack of familiarity with variations of the normal cells . . . [and] an abnormality in the number of interstitial cells was classified as: (1) hyperplasia—an increase of interstitial cells between the tubules without destruction or displacement of the tubules beyond the limits of the tumor; (2) local tumor—a discrete nodule or group of interstitial cells locally replacing or displacing the seminiferous tubules; and (3) malignant tumor—increase of interstitial cells with anaplasia, destruction of tubules and metastases."

In conformity with the generally accepted practice to call all grossly visible proliferations of germinal cells and sustentacular cells tumors, I call similar nodules of interstitial cells tumors. Admittedly, this is an arbitrary decision.

Dog. Dow (1962) reported that 24 of 56 dogs with interstitial cell tumors had bilateral involvement and that the neoplasms were often multiple. He stated that "The individual lesions ranged from 1 or 2 mm up to 7 cm in diameter; 46 of them measured more than 1 cm, but only 16 of them exceeded 2 cm in diameter. The range in size was similar in both solitary and multiple nodules, but the majority of the larger specimens appeared to be single."

Canine interstitial cell (IC) tumors seldom occur in retained testes. Scully and Coffin (1952) reported the presence of an interstitial cell tumor in one cryptorchid among 45 dogs with this neoplasm. Lipowitz *et al.* (1973) reported interstitial cell tumors in 67 dogs. The affected testes were in the scrotum in 63 dogs, and the location of the tumors was not recorded in 4 animals. "Associated clinical changes were found in 59 (88%) of the dogs with IC tumors; of these dogs, prostatic disease was diagnosed in 20 (30%), perianal gland adenomas in 25 (37.3%) and perianal gland adenocarcinomas in 6 (9%). Perineal hernias were found in 10 dogs (15%) in this group. Only one dog had evidence of alopecia, and none had gynecomastia or pendulous penile sheath." (Lipowitz *et al.*, 1973). They concluded that interstitial cell tumors in the dog are associated with an increase in androgen production.

Estrogen production by interstitial cell tumors occurs in some dogs. Kahan (1955) reported alopecia, swelling of the penile sheath, and enlargement of the nipples in a dog with an interstitial cell tumor and testicular atrophy. Following castration, "the patient made a good recovery, no longer attracted other males, the gynecomastia receded, and the hair grew back over the denuded areas."

Laufer and Sulman (1956) reported a case of feminization in a 7-year-old Boxer with an interstitial cell tumor. The dog had gradually shown signs of feminization over a 2-year period. The nipples became enlarged, the prepuce became pendulous, and there was a loss of hair on the thighs and neck. "The skin of the depilated areas appeared smooth, pliable, and somewhat thinner than normal." The dog urinated in a typical female position and attracted other male dogs. The left testis, which was located in the inguinal

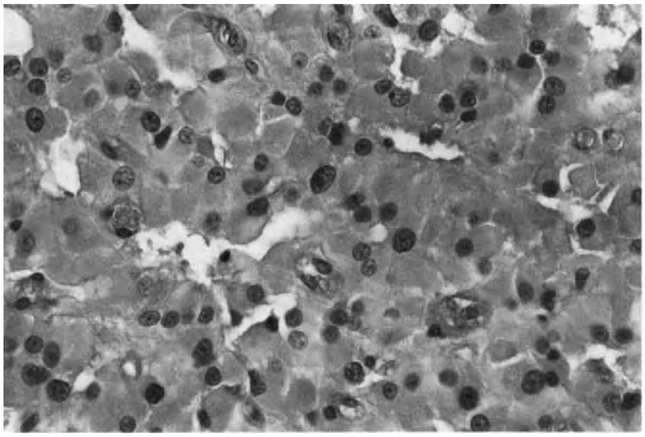

Fig. 15.2. Canine interstitial cell tumor. Note the considerable variation in size of nuclei. ×385. Acc. No. 8061.

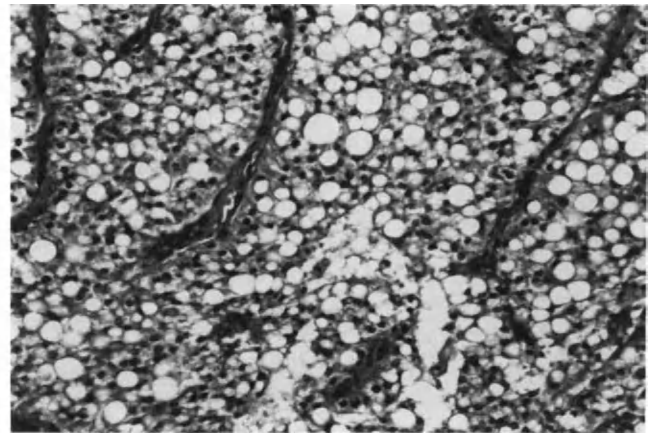

Fig. 15.4. Canine interstitial cell tumor with large cytoplasmic vacuoles. × 178. Acc. No. 20514.

region and contained a tumor, was removed surgically. It contained a 3 × 4-cm interstitial cell tumor. The signs of feminization persisted for 2 years and increased during the last year. "Later on, the animal showed a peculiar inclination for roaming, like a female dog in heat." The dog developed ataxia with transient disorientation, indicating cerebellar metastasis, and the animal was killed. The right testis contained multiple nodules of interstitial cell tumors that were 0.5 to 1.0 cm in diameter. A 2.0-cm interstitial cell tumor was present in the cerebellum.

Cotchin (1960a) reported alopecia, feminization, or alopecia and feminization in 16 aged dogs with interstitial cell tumors. Hair regrowth was recorded for three of the dogs following surgical removal of the neoplastic testes. The results of surgery were not known for most of the other cases.

Interstitial cell tumors of the canine testis are soft spherical masses of tan, yellow to orange tissue. The tumors are well demarcated from the surrounding tissue. Multiple neoplastic nodules are often present. Occasionally the tumor completely replaces the seminiferous tubules and large cysts may be present. Some of the larger neoplasms have areas of necrosis and hemorrhage because blood vessels are usually the only supporting tissue. Thus the tumors are subject to traumatic injury.

Histologically, the tumors consist of enlarged interstitial cells arranged in sheets or cords supported by a delicate network of thin-walled blood vessels. The neoplastic cells are usually polyhedral or rounded but may appear as columnar cells when they are adjacent to blood vessels. Cell outlines are usually demonstrable. All canine interstitial cell tumors contain cytoplasmic lipid that may be present as very fine or large vacuoles. The size of the lipid vacuoles may vary in different tumors and in various areas of a neoplasm (Figs. 15.2, 15.3, and 15.4). Large vascular spaces may be present (Fig. 15.5).

Scully and Coffin (1952) reported that the fat vac-

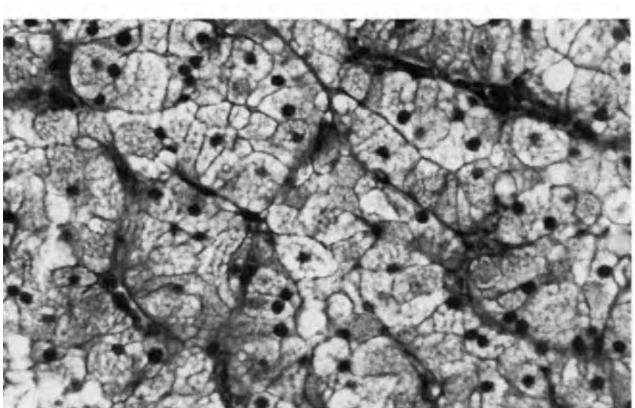

Fig. 15.3. Canine interstitial cell tumor with numerous small cytoplasmic vacuoles. ×222. Acc. No. 8052.

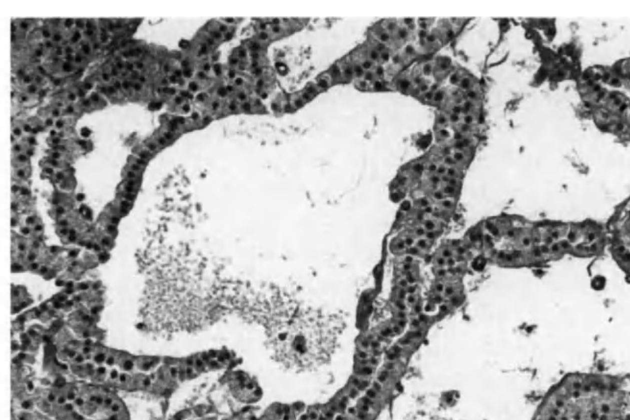

Fig. 15.5. Canine interstitial cell tumor with large vascular spaces. × 178. Acc. No. 18316.

uoles "show pale green autofluorescence, are birefringent, stain bright orange with Scharlach R, and deep blue (positive) with Asbel and Seligaman's stain for carbonyl groups—reactions said to be characteristic of steroids. In addition to fat, some Leydig-cell tumors show a considerable cytoplasmic content of yellow lipochrome." The nuclei of the neoplastic cells are round to oval and may vary in size, whereas normal interstitial cells are quite uniform. Mitoses are rare in the benign tumors.

von Bomhard *et al.* (1978b) compared the ultrastructure of normal canine interstitial cells with that of neoplastic cells. The cells of most interstitial cell tumors showed the typical characteristics of normal interstitial cells, including "abundant smooth endoplasmic reticulum, mitochondria with tubular inner structures and numerous small and larger granules, many lipid droplets, intracytoplasmic filaments, and oval nuclei with distinct nuclear pores."

Bull. Innes (1942) described a benign interstitial cell tumor that was present in the left testis of a 3-month-old calf. The testis was removed surgically because it was enlarged. All the testicular parenchyma was replaced by one small and three large tumor nodules. The normal structure of the testis had been replaced by "polyhedral cells with small spherical nuclei resembling the large interstitial variety. They formed compact masses with numerous fibroblasts and blood vessels. In other areas, cords of tumor cells radiated out from vessels very much in the manner of hepatic cells. The cytoplasm was either lightly stained and foamy or intensely eosinophilic" (Innes, 1942). Abundant lipid was present in the foamy cells but not in the eosinophilic cells. The calf grew normally and was sold as a yearling.

Rangel and Machado (1952) reported an interstitial cell tumor in the left testis of a 6-year-old hybrid Brahma bull. The bull was "used as a draft animal after castration by inversion and torsion of both testes into the scrotal pouches." Following castration, the bull was sexually active and a smaller than normal left testis was palpated in the scrotum. Sexual activity ceased after surgical removal of the testis. The cut surface of the testis consisted of brown greasy tissue. Microscopically, the tissue consisted of lobules of large round to polyhedral cells with granular vacuolated cytoplasm.

Munro (1955–1956) reported interstitial cell tumors of the testis in an Ayrshire and a Guernsey bull. The "bulls showed poor semen density and poor service behavior but a varying incidence of abnormal sperm." Cupps *et al.* (1964) recorded interstitial cell tumors in three bulls with testicular degeneration and hypertrophy of the glomerular zone of the adrenal cortex.

Dunn and McEntee (1964) compared the semen quality and fertility records of 20 artificial breeding sires that had interstitial cell tumors with similar records from 20 bulls that were slaughtered mainly because of low milk production by their daughters. The controls were paired with tumor bulls according to age and bred. The ages of the 40 bulls ranged from 7 to 15 years. The records of semen quality of the last 12 ejaculates of each bull were examined. "The criterion of fertility was the percentage of first-service cows, inseminated with the last 12 usable samples of semen, which did not return to service during a 60- to 90-day period following service" (Dunn and McEntee, 1964).

The incidence of interstitial cell tumors according to breed was: Guernsey, 10 of 52 bulls; Holstein, 4 of 96; Jersey, 3 of 30; Ayrshire, 2 of 25; and Brown Swiss, 1 of 13. The affected bulls had a larger volume of semen and a lower percentage of motile sperm than normal bulls, but the differences were not statistically significant. The tumor bulls had significantly fewer sperm per milliliter of semen than the normal bulls. The bulls with testicular tumors had 47 substandard ejaculates with poor motility, concentration, or both. Only 7 of 246 samples from normal bulls were rejected as substandard, and 4 of these were from a senile bull, 15 years old, suffering from severe arthritis. The 60- to 90-day nonreturn rate of the cows bred to tumor bulls was 1.7 percentage units lower than that for the controls–a highly significant difference.

"For the purpose of comparing the size of each bull's tumor mass with semen quality and fertility, the sum of the diameters of the individual tumor nodules was used. . . . Any bull with sum of tumor diameters greater than 1.0 cm was classified as having a large interstitial cell tumor" (Dunn and McEntee, 1964). Eight of the bulls were classified as having large tumors. The sperm production and fertility of these bulls were significantly lower than those in other bulls of similar age and breed ($P < 0.01$). Bulls with small interstitial cell tumors did not have a significant degree of inferior semen quality nor infertility.

In addition to the 20 cases of testicular tumors that have been discussed, I have seen an additional 23 cases from the same bull stud and 3 from other sources.

A sharp line of distinction cannot be drawn between hyperplasia and neoplasia of testicular interstitial cells in the bull. Thus (as stated previously), I consider all grossly visible nodules of interstitial cells in the bovine testis to be neoplastic. If a bull is kept for many months beyond the time when his fertility has decreased, the neoplastic tissue will replace most of the seminiferous tubules and the gonad will become larger than normal.

Small bovine tumors, which range from about 3 to 6 mm in diameter, are pale gray, circumscribed nodules of slightly firm tissue that bulge slightly above the cut surface. The large neoplasms are yellow-gray to orange, spherical, and well demarcated from surrounding tissue (Fig. 15.6). They are comparatively soft and bulge considerably above the cut surface. The largest bovine interstitial cell tumor that I have seen completely replaced the normal right testis and weighed 673 g. The left testis weighed 313 g and contained a 5.3 × 6.5-cm tumor (Fig. 15.7).

The tumors consist of densely packed, polyhedral to rounded cells that are quite similar to normal interstitial cells (Fig. 15.8). The cytoplasm is abundant and more intensely eosinophilic than normal. In contrast to the neoplasms in the dog, there is a striking absence of vacuolation of the cytoplasm and very little lipid is present. The bovine tumors are much more uniform in histologic appearance than those of the dog.

Stallion. Interstitial cell tumors of the equine testis have been reported by Stenström (1918), Peyron (1921), Ball and Douville (1926), Pallaske (1931), Smith (1954), and Gelberg and McEntee (1987). Stenström described a 1650g testicular tumor from a 14-year-old horse. The tumor described by Smith occurred in an abdominal testis of a 7-year-old saddle horse. A descended testis had been removed early in life. The stallion showed "troublesome characteristics of masculinity," and thus the retained testis was removed. It measured about 1.5 × 2.0 × 2.5 cm. The tumor consisted of clumps of large oval interstitial cells in bands of fibrous tissue. Granules of golden yellow pigment were present in the cytoplasm of the interstitial cells. Scarlet red stain revealed the presence of fat, which was anisotropic under the polarizing microscope.

I have examined similar interstitial cell lesions from nine stallions. These cases have been reported by Gelberg and McEntee (1987). All but one of the affected horses were unilateral or bilateral cryptorchids. Only two were reported to have been fertile and only one of these had two scrotal testes. This horse had good fertility until it was about 9 years old. Then its fertility decreased to a very low level during the next 3 years, and it was killed. The left testis weighed 24 g and the right 80 g. Both testes were dark and contained pale areas that consisted of well

Fig. 15.7. Large bilateral interstitial cell tumors from a 10-year-old, sterile, Guernsey bull. Acc. No. 2549.

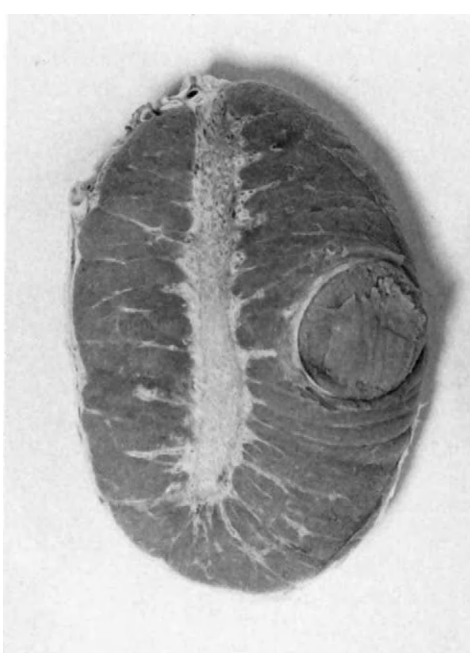

Fig. 15.6. Midsagittal section of testis from a 12 1/2-year-old Guernsey bull with a 4-cm interstitial cell tumor. Acc. No. 1199.

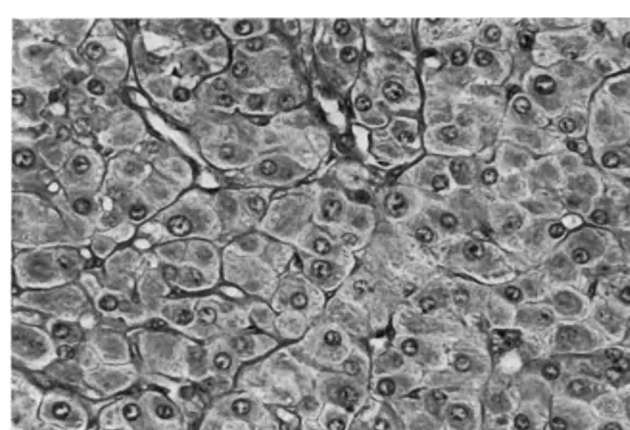

Fig. 15.8. Bovine interstitial cell tumor with uniform population of neoplastic cells. ×259. Acc. No. 1199.

differentiated and immature interstitial cells in a fibrous tissue stroma. The interstitial cell tumors in the other eight stallions occurred in abdominal or high flanker testes. The ages of the affected animals ranged from 3 to 20 years. The breeds included Morgan, Thoroughbred, Belgian, Shetland Pony, and crossbred. The breed of two horses was not recorded.

A 3-year-old horse with bilateral tumors was a male pseudohermaphrodite with retroflexion of the penis. A 20-year-old stallion with bilateral neoplasms became vicious, injured a man's chest, and picked a girl up by the hair. The signs of viciousness gradually disappeared following castration. No clinical signs, other than stallionlike behavior, were recorded for the rest of the horses.

The tumors were bilateral in five horses and unilateral in four. The weight of the affected testes ranged from 12.4 to 80 g and averaged 32.8 g. Since none of the affected testes were very large and a number of the horses were old, it appears that the tumors grew very slowly. Some of the interstitial cell tumors of the equine testis have undoubtedly been overlooked because the gonads are small, clinical signs are usually absent, and pathologists do not routinely examine testes from castrated horses. All the tumors were visible on gross examination of the cut testis. The tumors consisted of multiple, firm, gray, irregular-shaped nodules, up to about 2 cm in diameter, that blended into the adjacent testicular tissue.

The tumors consisted of a mixture of mature interstitial cells, some of which contained brown cytoplasmic pigment granules, immature interstitial cells, fibroblasts, and blood vessels. Degenerate seminiferous tubules were trapped in the periphery of the tumors. There was not as sharp a demarcation between the proliferative lesions and the rest of the testes as is present in interstitial cell tumors in other species of domestic mammals. Perivascular lymphocytic foci were present in some of the neoplasms as well as in the adjoining testicular tissue.

Cat. Cotchin (1984) reported three testicular neoplasms that were found in domestic cats. They included "a possible seminoma" in a 13-year-old and interstitial cell tumors in two old cats. The lesions were not described.

I have seen only one feline testicular neoplasm—an interstitial cell tumor in a 13-year-old cat. The tumor was an incidental finding at necropsy. The midsagittal section of the testis measured 11 × 13 mm and the tumor 5 × 9 mm. Normal spermatogenesis was present in the nonneoplastic portion of the gonad. The tumor did not have a capsule, was well demarcated, and consisted of densely packed interstitial cells. The supporting stroma consisted of thin-walled blood vessels. The neoplastic cells were much larger than normal interstitial cells and they had distinct cell boundaries. The eosinophilic cytoplasm contained vacuoles of various sizes. Large eosinophilic bodies were present in the cytoplasm of a few cells. The nuclei were larger than those of the normal interstitial cells, contained a single prominent nucleolus, and were located eccentrically. Mitotic figures were not seen.

Other Species. I am not aware of reports concerning interstitial cell tumors in the ram, goat, or boar.

Seminoma (Germinal Cell Tumor, Spermatogonioma)

The seminoma is a neoplasm of the germinal cells of the testis and is the counterpart of the ovarian dysgerminoma. Seminomas occur most frequently in the dog and have been reported to occur in the stallion, ram, bull, goat, and cat.

The main clinical sign manifested in domestic mammals with seminomas is enlargement of the affected gonad. Thus most small tumors of the seminiferous epithelium are overlooked on clinical examination. The pathologist overlooks intratubular seminomas when the testes are not examined histologically.

Seminomas have less gross and histologic variation among the various species of domestic mammals than do interstitial cell tumors. The cut surface of a fresh specimen bulges above the adjacent testicular tissue. The neoplasms are white to gray, glistening, and soft to slightly firm depending on the amount of fibrous tissue stroma. Large neoplasms may be lobulated and may contain areas of hemorrhage and necrosis (Fig. 15.9).

Histologically, the seminoma starts as an intratubu-

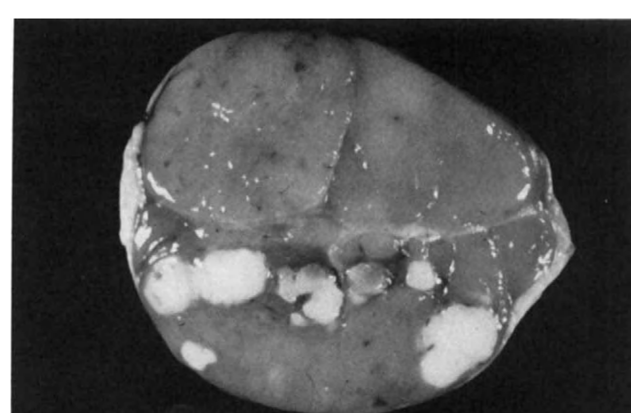

Fig. 15.9. Canine seminoma with glistening surface. White areas are foci of necrosis. Acc. No. 18542.

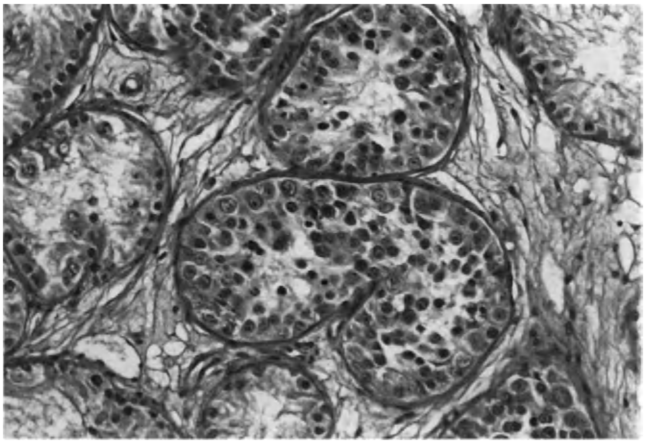

Fig. 15.10. Intratubular seminoma in a canine testis. ×178. Acc. No. 19371.

lar growth of neoplastic germinal cells (Fig. 15.10). Proliferation of the tumor cells eventually results in destruction of the tubular wall and the formation of a diffuse neoplasm. The tumor is frequently multifocal and may occur in scattered areas throughout the testis. The cytoplasm of the neoplastic cells is scant and slightly basophilic. The cell boundaries are usually indistinct. The nuclei vary in size (Fig. 15.11) and mitotic figures are often numerous. Large foci of lymphocytes are present in many of the neoplasms. Histologically, the neoplasm appears to be malignant but relatively few of the canine tumors metastasize.

Dog. During a survey of testicular tumors in dogs, Dow (1962) found that "almost one in nine of all dogs over the age of four years were found to have a seminoma and that in less than one-third was this detectable on clinical examination, the testis being considered normal in 32 out of the 45 dogs affected with this tumor. Systemic symptoms due to the testicular tumor were not observed in any case, but two dogs with co-existent Sertoli cell tumors showed feminization."

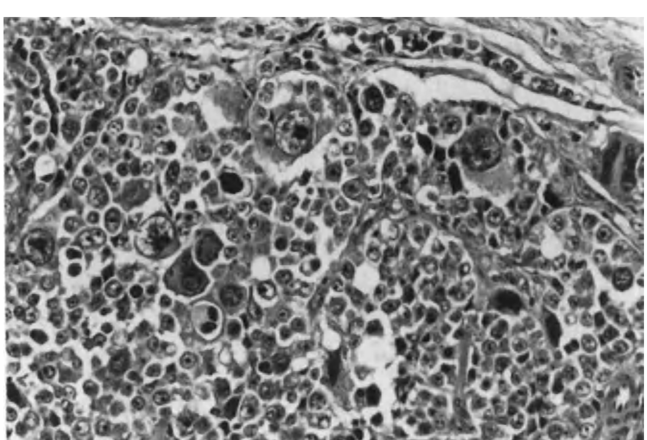

Fig. 15.11. Canine seminoma with large variation in size of the neoplastic cells. ×178. Acc. No. 17348.

Metastatic lesions were found in four dogs. Dow stated that "As yet no definite criteria for the diagnosis of malignancy in canine seminomas have been formulated and this section describes only those cases in which metastases were present. The four primary tumors were all large masses measuring from 5 to 10 cm in diameter and replacing the entire testis. They show a close morphological resemblance to the diffuse infiltrative type of tumor and are composed of large sheets of cells divided up into irregular lobules by a variable number of relatively inconspicuous fibrovascular trabeculae." Bizarre mitoses and numerous mitotic figures were present. The lymphatics and veins of the testis were invaded in all the malignant cases and the tunica albuginea and epididymis were invaded in some. Metastatic lesions were present in the internal iliac lymph nodes in two dogs and in the lung, internal iliac, and paraaortic lymph nodes of another dog.

Cotchin (1960a) reported seminomas in 107 dogs. Most of the tumors were surgical specimens. The age was recorded for 89 of the affected dogs, and it ranged from 2 to 18 years with an average of 10 years. The tumor was reported to be in an ectopic testis in 18 of 69 dogs. The chief clinical sign shown by dogs with seminomas was enlargement of the affected testis. The clinically recognized duration of the tumors in 29 dogs varied from 3 days to 4 years with an average of 9 months. The size of the tumors varied from 1 to 11 cm (average 6.3 cm). Perivascular lymphocytic foci were present "in at least 72 seminomas. They are sometimes scanty but sometimes very numerous. There is no correlation between their number and the size of the tumour except that perhaps the most marked accumulations are seen in and near small seminomas" (Cotchin, 1960a).

Sagartz and Robinson (1972) reported seminomas with metastases in two dogs. They stated that "There are no reliable histopathologic criteria for the diagnosis of malignancy of canine seminomas so that all cases should be regarded as potentially malignant even though malignancy is quite rare." Presumably they meant that it is not possible to diagnose malignancy by merely examining a section of the neoplasm. Malignancy can be diagnosed by examining sections of the testicular tunic, epididymis, spermatic cord, and regional lymph nodes. The problem of diagnosing malignancy arises when the examination is restricted to only a section of the neoplasm.

Comhaire *et al.* (1974) reported an increase in the concentration of estradiol in the peripheral plasma of three dogs with seminomas. Two of the dogs had an elevated concentration of the hormone in the spermatic vein blood draining the neoplastic testis. They concluded that seminomas as well as sustentacular cell tumors can produce estradiol. However, the dogs did not have clinical signs of feminization.

Barsanti *et al.* (1979) reported the occurrence of bilaterally symmetrical truncal alopecia and hyperpigmentation of the skin in a dog with a small seminoma in one testis. The level of serum testosterone was "markedly less than normal," but the level of estrogens was not determined. Hair growth returned following castration. The data presented do not provide conclusive evidence that the seminoma was the cause of the hair loss.

Stallion. Seminomas and interstitial cell tumors are the most common testicular neoplasms in aged stallions. Seminomas are reported more frequently because the tumors usually occur in inguinal or normally descended testes that become markedly enlarged. In comparison, interstitial cell tumors of the horse usually occur in retained testes and do not cause marked enlargement of the testis. The gross and histologic appearance of equine seminomas is similar to that of the dog (Figs. 15.12, 15.13, and 15.14).

Kimura (1917) recorded 114 neoplasms in 77,224 slaughtered horses in Japan. Testicular tumors were found in 49 animals and melanomas in 36. He reported that the testicular neoplasms were found predominantly in old stallions and usually only one testis was involved. The size of the tumor was variable but generally it was "as large as the human head." Metastases were frequently found in the spermatic cord and in the inguinal and lumbar lymph nodes. Apparently most of the testicular neoplasms were seminomas. From this report, it would appear that the seminoma is the most common testicular neoplasm in old stallions. However, interstitial cell tumors of the testis could be overlooked in a slaughterhouse survey because the affected testes do not generally become markedly enlarged.

It appears that equine seminomas have a greater tendency to metastasize than those of the dog. Malignant seminomas in the stallion have been recorded by Becht *et al.* (1979), Vaillancourt *et al.* (1979), Hedjazi and Naghshineh (1981), Pandolfi and Roperto (1983), Gibson (1984), and Trigo *et al.* (1984).

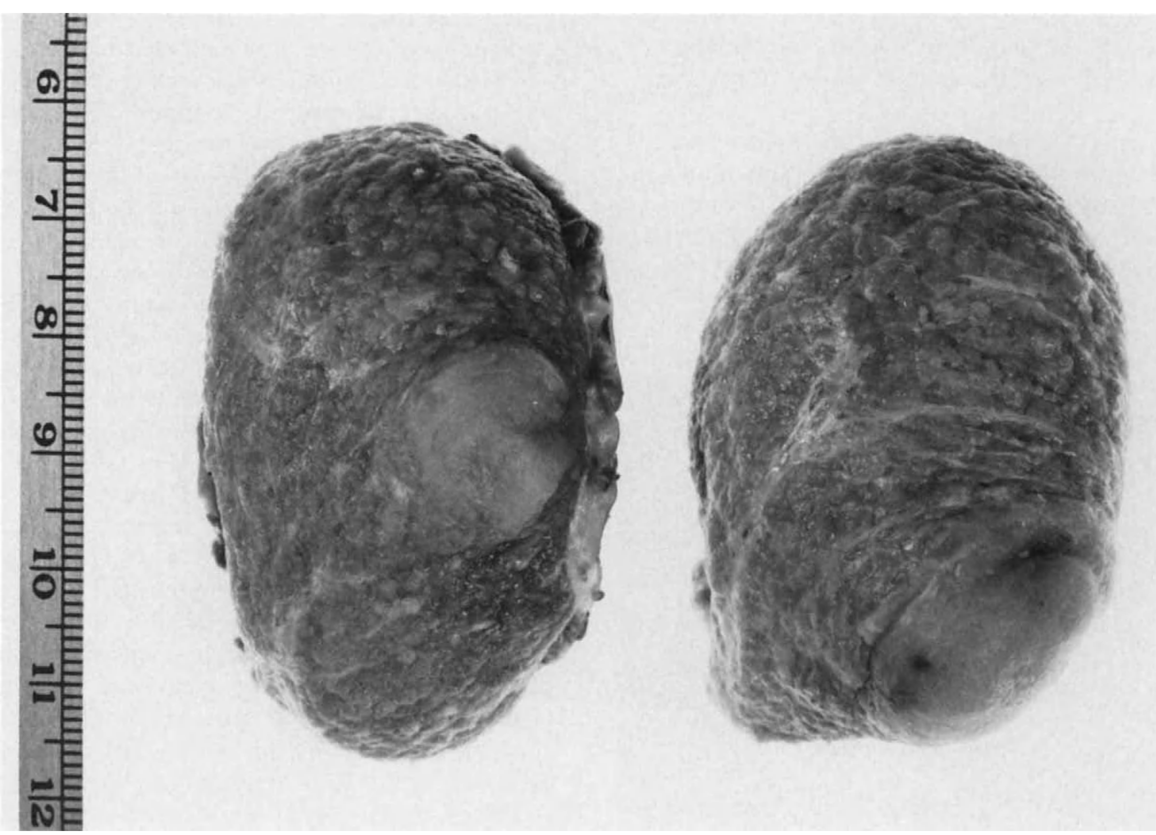

Fig. 15.12. Bilateral seminomas from an 18-year-old Morgan stallion. Centimeter rule. Acc. No. 13472.

Fig. 15.13. Unilateral seminoma from a 16-year-old Welsh pony. Tumor replaced most of testis and weighed 1257 g. Acc. No. 7367.

Ram. Jensen and Flint (1963) reported bilateral intratubular seminomas in five rams that varied in age from 5 to 8 years. "In no case had the neoplasm progressed to a size sufficient for gross detection. A review of the literature revealed no previous reports of seminomas in sheep."

Shortridge and Cordes (1969) reported unilateral seminomas in two rams from New Zealand. The tumors caused enlargement of the affected gonads. "In one case the neoplasm infiltrated the interstitial tissue of the epididymis and spermatic cord. In both cases the neoplasm had penetrated veins and lymphatic vessels." No other tissues were submitted for examination, thus it could not be determined whether other metastatic lesions were present.

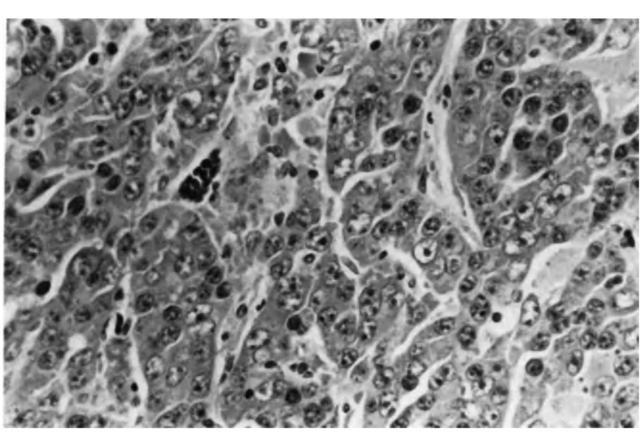

Fig. 15.14. Seminoma from an 18-year-old stallion. ×231. Acc. No. 13472.

Watt (1971) found one bilateral seminoma in an aged ram during the examination of the testes of 2281 Merino rams from an abattoir in Western Australia. Both testes were smaller and firmer than normal. Histologic examination "revealed large numbers of neoplastic cells occupying many swollen seminiferous tubules and invading the interstitial tissue."

Bull. Bovine seminomas appear to be quite rare. They have been recorded by Sedlmeier (1926), Montpellier and Poisson (1929), Drieux and Mendoza (1937), and Bhagwat *et al.* (1972). Although I have seen many interstitial cell and sustentacular cell tumors in bulls, I have not had the opportunity to examine a bovine seminoma.

Goat. Pamukcu (1954) reported a seminoma that occurred in a goat.

Cat. Cotchin (1984) recorded a "possible seminoma" in a cat. Carpenter *et al.* (1987) reported the occurrence of a malignant seminoma in a 2-year-old domestic shorthair cat with bilateral retained testes. A 6-cm tumor was present in the left testis. The cat was killed 1 year later because it was obstipated and sublumbar masses were palpated. It was found to have metastatic seminomas in the lymph nodes and soft tissues of the sublumbar region.

Sustentacular Cell Tumor (Tubular Adenoma and Adenocarcinoma, Sertoli Cell Tumor)

The sustentacular cell tumor is a neoplasm of the supporting cells of the seminiferous tubules. These neoplasms occur most frequently in the dog and have been reported to occur in the bull, stallion, ram, and cat. Sustentacular cell tumors can usually be diagnosed on gross examination because they are pale gray, nodular, firm to very firm neoplasms with irregular-shaped invaginations of the neoplastic tissue into the adjacent testicular parenchyma.

The neoplastic cells frequently resemble normal sustentacular cells and are usually packed into islands or tubules between bands of fibrous tissue (Fig. 15.15). There is a wide range in the morphology of the neoplastic cells. Scully and Coffin (1952) stated that the tumor cells "range in shape from round or polyhedral to tall and slender. Usually their cell boundaries are indistinct, the nuclei lying in a sleazy eosinophilic cytoplasmic syncytium. On the other hand, the cytoplasm may be compact and deeply eosinophilic." The nuclei may be round, oval, or spindle-shaped. Small cysts are present in the center of the islands of tumor cells in some neoplasms.

Dog. Cotchin (1960a) reported sustentacular cell tumors in 157 dogs. Most of the affected testes were surgically removed. The ages of the dogs ranged from 3 to 15 years (average 8 1/2 years). For cases in which the location of the affected testis was recorded, sustentacular cell tumors were present in retained testes in 65 (58%) of 112 dogs. Forty-five (28.7%) of 157 dogs had alopecia, feminization, or both alopecia and feminization (Fig. 15.16). "Favored sites for the development of the alopecia were under the thorax and abdomen, inside the thighs, on the flanks and on the sides of the chest and neck and near the root of the tail. The feminization was shown partly by changes in behaviour and partly by changes in appearance. The chief sign noted was that the affected dog appeared to become as attractive to other male dogs as if it were a bitch in season." (Cotchin, 1960a). The prepuce became flabby and pendulous and the teats became enlarged. Some dogs became pot-bellied. The nonneoplastic descended testis was usually atrophic. Metastatic lesions were recorded for only two dogs with sustentacular cell tumors: in the kidney in one and in the liver and lung in the second. Although the regional lymph nodes were not mentioned, they were probably affected.

Dow (1962) reported clinical signs of feminization in 6 of 36 dogs with sustentacular cell tumors. His material differed from that reported by Cotchin (1960a) in that he examined testes from 580 unselected adult dogs submitted for necropsy. Thus some of the tumors were undoubtedly in an early stage of development. Two of the dogs attracted other male dogs. "The affected testis was grossly enlarged and the other was small and flaccid in all of the six dogs with evidence of oestrogen activity. The remaining 30

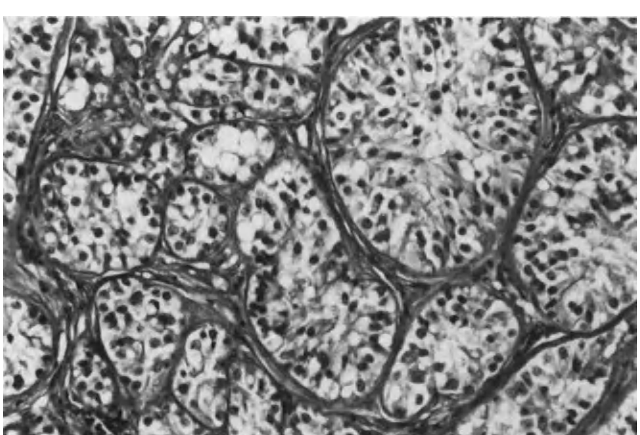

Fig. 15.15. Canine sustentacular cell tumor. Neoplastic cells have pale, streaming cytoplasm and uniform-sized nuclei. Bands of fibrous tissue surround the islands of sustentacular cells. ×178. Acc. No. 16502.

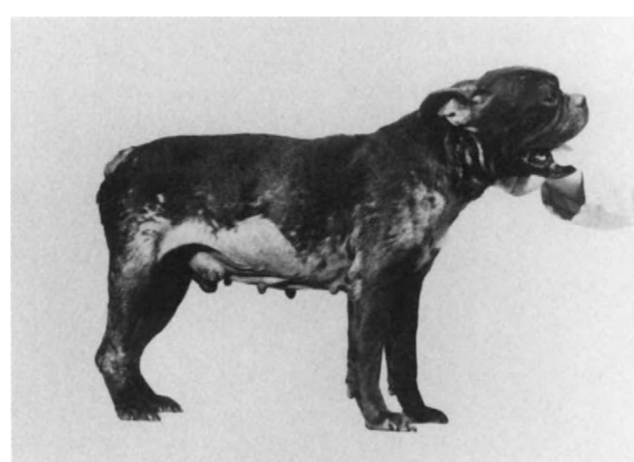

Fig. 15.16. French Bulldog with ventral hair loss, edema of prepuce, and enlargement of nipples due to estrogen-producing sustentacular cell tumor. Acc. No. 982.

dogs exhibited no hormonal symptoms. Testicular enlargement was noted in only nine of them, and atrophy of the contralateral testis was recorded in only two dogs" (Dow, 1962). Metastatic lesions were found in the internal iliac lymph nodes in five cases. The primary tumors in these cases were large and had completely replaced the normal testicular tissue. In addition to metastases in the iliac lymph nodes, metastatic lesions were found in the epididymis, spermatic cord, paraaortic lymph nodes, lungs, liver, kidney, and spleen. Metastases were not found in all of these organs in every dog.

Hauser and Wild (1978) reported the presence of intracellular and extracellular bodies in sustentacular cell tumors in dogs. They stated that "numerous tumor cells, mainly in the periphery of the tubules, contained intracytoplasmic round eosinophilic inclusions which stained intensely with PAS. Towards the center of the tubules the size of the bodies increased and they became extracellular." The significance of the bodies was not established. Similar bodies have been reported in sustentacular cell tumors of the bull (Ladds and Saunders, 1976), in the sex cords of freemartins (Herzog, 1967), and in the sustentacular cells of the testes of prepuberal goats (Widmaier, 1959).

Scully and Coffin (1952) reported the occurrence of sustentacular cell tumors in 28 dogs with an age range of 4 to 16 years (average 10 years). The tumors were bilateral in two animals. Metastatic lesions were found in the sublumbar lymph nodes in two cases. Clinical signs of hyperestrogenism were observed in eight dogs that had large tumors. They stated that "In general, the smaller tumors have an innocent microscopic appearance, while the larger ones are apt to have cancerous characteristics."

Brodey and Martin (1958) examined 37 dogs with sustentacular cell neoplasms. The age range of the affected dogs was 3 to 20 years, and the average was 9.3 years. Twenty dogs had alopecia that tended to be symmetrical, involving primarily the ventral thorax and abdomen and the posterior and lateral aspects of the thighs. The hair was rather dry and brittle and was pulled out easily. The skin was thin and velvety. Sixteen dogs had gynecomastia. The feminized dogs had atrophy of the prostate in some cases and enlargement in others; some had a flaccid, pendulous prepuce. The neoplasms were in the right testis in 22 dogs, in the left in 5, and bilateral in 4 of the 31 dogs on which the information on location was available. Neoplastic testes were in the abdominal cavity or in the inguinal region in 20 animals. The neoplasms were outside of the scrotum in 81% of the dogs showing gynecomastia. The tumors had metastasized in 4 (12.9%) of the dogs.

Streett (1967) reported a malignant sustentacular cell tumor that occurred in a 6-year-old Beagle. The owner noticed that the dog's scrotum was greatly enlarged, but no other clinical sign of disease was noted. The enlarged right testis was removed surgically and the left testis was not removed. The right testis was nodular, firm, and whitish gray. "The spermatic veins were very tortuous and had a very large diameter (2 cm) at certain points" (Streett, 1967). The neoplasm was diagnosed as a malignant sustentacular cell tumor. The dog made an uneventful recovery. However, it was returned to the veterinary hospital about 3 1/2 months later because the owner noticed that the dog had not been eating for 2 or 3 days, was listless, and was attracting male dogs. The dog walked with a stiff gait, the abdomen was very tense, and a firm nodular mass was felt in the caudal lumbar region. The dog seemed to be in considerable pain at times and was killed. Metastatic sustentacular cell tumors were found in the sublumbar lymph nodes, spleen, mediastinum, adrenal, and spinal canal.

Reif and Brodey (1969) reported that 58 (53.7%) of 108 canine sustentacular cell tumors occurred in cryptorchid testes. They stated that there appears to be a relationship between the location of the neoplastic testis and the occurrence of feminization. "Feminization was evident in 16.7 percent of the dogs with scrotal SCT (sustentacular cell tumors), 50.0 percent of dogs with inguinal SCT and 70.4 percent of dogs with abdominal SCT. Perhaps the differences in malignancy might be explained by the fact that the tumors in retained testes, which were hidden from view, had the opportunity to be present for a longer period of time and became larger than neoplasms in scrotal testes. Malignancy is more common in the larger neoplasms" (Reif and Brodey, 1969).

Some dogs with sustentacular cell tumors develop lesions in other organs as well as clinical signs of hyperestrogenism. Alterations may occur in the skin, epididymides, nonneoplastic testicular tissue, prostate, teats, mammary glands, kidneys, adipose tissue, bone marrow, and blood. There is a bilaterally symmetrical loss of hair that starts in the genital area, medial thighs, and ventral abdomen. As the condition progresses, the alopecia extends to the ventral thorax, dorsal sacral, and lumbar areas and to the neck and shoulders (Fig. 15.16). One of the first signs of the syndrome may be a failure of hair to regrow after clipping. There is thinning and increased pigmentation of the skin. The epididymal epithelium grows into and beyond the muscular wall but does not result in the development of sperm granulomas because the nonneoplastic testicular tissue atrophies under the influence of estrogen and is, therefore, not producing sperm. Inflammation and squamous metaplasia occur in the prostate gland. The teats enlarge and the mammary glands became hyperplastic. Squamous metaplasia may occur in the collecting tubules of the kidneys (Lindberg *et al.*, 1976). There may be a female distribution of adipose tissue, which sometimes becomes very excessive. Edwards (1981) and Sherding *et al.* (1981) reported bone marrow hypoplasia in dogs with sustentacular cell tumors.

Mucometra and pyometra may develop in hermaphroditic dogs with sustentacular cell tumors. Sustentacular cell tumors associated with cryptorchidism and male pseudohermaphroditism appear to occur more frequently in Miniature Schnauzers than in other breeds of dogs (Frey *et al.*, 1965; Norrdin and Baum, 1970; Lederer, 1975; Brown *et al.*, 1976). The anatomic features of the reproductive organs were similar in all reported cases. They had male external genitalia and retained testes and behaved as males until feminizing sustentacular cell tumors developed. It was not realized that the dogs were male pseudohermaphrodites until they were submitted to surgery. They had prominent uteri with cystic endometrial hyperplasia of the estrogenic type and squamous metaplasia of the prostate due to estrogen production by the sustentacular cell tumors.

Bull. Cotchin (1960b) described three tubular adenomas (sustentacular cell tumors) of the testes of newborn calves. The tumors measured 14 × 8 1/2, 7 × 5, and 16 × 7 1/2 cm.

Palmer *et al.* (1980) reported the occurrence of sustentacular cell tumors in two related newborn Shorthorn calves. The tumors occurred in single descended testes and opposite testes were not found. Possibly the bulls were monorchids.

I have examined sustentacular cell tumors from 26 bulls, 21 of which were from one artificial breeding center. The tumors were pale gray and firm and had an irregular surface (Fig. 15.17). The breed distribution of the 26 bulls was 17 Holstein-Friesian, 3 Swedish Red and White, 2 Guernsey, 1 Ayrshire, 1 Aberdeen Angus, and 2 unrecorded. The ages of the affected bulls varied from 1 to 12 years. Three bulls with large testicular neoplasms had metastatic lesions in the regional lymph nodes.

Ladds and Saunders (1976) conducted gross examination of the genital tracts of 1598 bulls killed in abattoirs in Australia. Tissue sections were prepared from testes when nodular lesions were observed on gross examination. Sustentacular cell tumors were found in one mature and five aged bulls. Five of the bulls were Shorthorns and one was presumed to be a Shorthorn × Santa Gertrudis crossbred.

Blom and Christensen (1982) reported a sustentacular cell tumor of the left testis and segmental aplasia of the ipsilateral epididymis in a Danish Red bull. Although the epididymal anomaly was diagnosed at 15 months of age, the bull was used for artificial insemination. He had normal semen and good fertility until

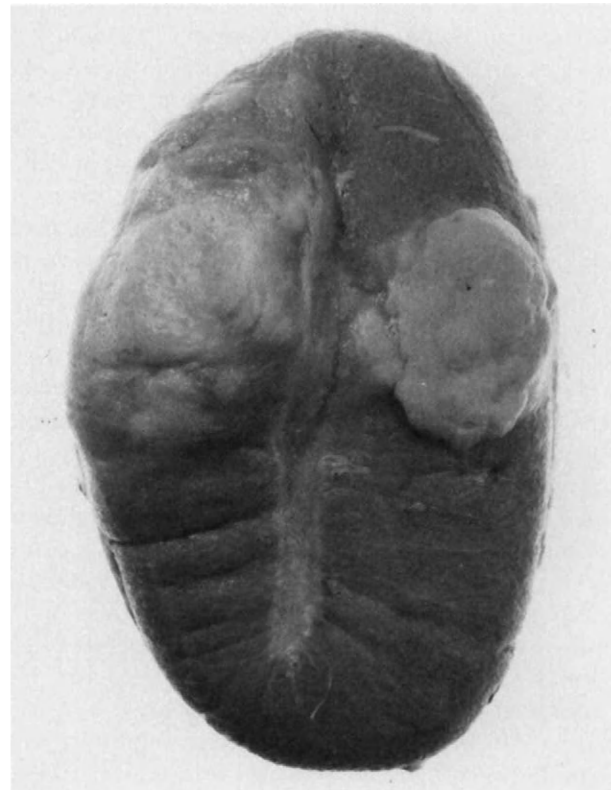

Fig. 15.17. Sustentacular cell tumors in testis of an 11-year-old Holstein bull. Acc. No. 12752.

the age of 11 years. The left testis was found to be smaller and firmer than the right on regular genital examinations. The semen quality became poor when the bull passed 11 years of age and the left testis was found to be enlarged. Within a few months the size of the testis was three to four times that of the right and was hard and nodular. The bull was slaughtered at 11 1/2 months of age. There was segmental aplasia of the left epididymis, ampulla, and vesicular gland. The right testis appeared normal and weighed 580 g. The left testis weighed 2300 g and only traces of the caput epididymis were present. The left corpus and cauda epididymis were missing. The cut surface of the left gonad revealed that the testicular tissue had been replaced by multiple, white to yellow, rather soft nodules of varied size. The histologic appearance of the testicular neoplasm was characteristic of a sustentacular cell tumor. The regional lymph nodes were not sectioned, but gross examination did not reveal evidence of metastases.

Stallion. The sustentacular cell tumor appears to be rare in the horse. Rahaley *et al.* (1983) reported a case that occurred in an 11-year-old Quarter Horse stallion that was in poor condition and "failed to breed during the last two seasons. . . . The stallion had ventral abdominal alopecia without dermatitis but had no discernible teat development nor was it attractive to other stallions." The right testis was soft and located in the inguinal canal. The left testis was small and contained a 2-cm, firm, white, sustentacular cell tumor. The horse was disposed of shortly after castration but a necropsy was not performed.

Stickle and Fessler (1978) reported a sustentacular cell adenoma in an abdominal testis of a horse.

Ram. Shortridge (1962) recorded a sustentacular cell tumor in a ram. The neoplasm measured 1.5 × 3 cm and was cream-colored and nodular.

Cat. Meier (1956) described sustentacular cell tumors in two cats of unknown age. No signs of feminization were noticed. The neoplasm had metastasized to the liver and spleen in one cat. The other cat had a seminoma *in situ* in addition to the sustentacular cell neoplasm, which was considered to be malignant.

Mixed Germ Cell–Sex Cord–Stromal Neoplasm (Gonadoblastoma)

According to Mostofi and Price (1973), the gonadoblastoma of man is a "tumor forming a distinct mass and contains an intimate mixture of abnormally proliferating germ cells and immature or mature granulosa and/or Sertoli cells, with or without Leydig, theca, or lutein-like cells." These neoplasms were first reported by Scully (1953). He reviewed 74 cases and stated that all the affected individuals were sexually abnormal (Scully, 1970): "The gonad bearing the tumor was generally of indeterminate nature but was sometimes identifiable as a streak or a dysgenetic cryptorchid. Four-fifths of the patients were phenotypic females, who almost always had cryptorchidism, hypospadias, and female internal secondary sex organs. Eighty-nine percent of the patients were chromatin-negative, and the most common karyotypes were 46,XY and 45,XY/46,XY." Hughesdon and Kumarasamy (1970) reported the occurrence of this neoplasm in normally differentiated testes and ovaries.

Turk *et al.* (1981) reported the occurrence of a tumor resembling a gonadoblastoma in the left testis of a 15-year-old Shetland Sheepdog. They stated that "This neoplasm was characterized by discrete intratubular aggregates of intimately mixed germ cells and smaller cells resembling Sertoli cells. The latter small cells often formed a single cell layer surrounding the margin of eosinophilic, PAS-positive Call–Exner-like bodies. Electron microscopy showed these bodies to be composed of whorled laminae resembling basement membrane."

Cullen *et al.* (1987) reported a mixed germ cell–sex cord–stromal neoplasm that was found in a 10-year-old Arabian stallion. A 4 × 2-cm sessile mass was present in the dorsolateral aspect of the left testis. "The mass was discrete, encapsulated, and easily separated by blunt dissection from the adjacent testicular parenchyma. The cut surface was homogenous, pale grey, and firm." The tumor consisted mainly of a mixture of sustentacular cells and germ cells with the former predominating. Mitotic figures were present in some of the germ cells. "Infrequently foci of polyhedral eosinophilic cells that resembled interstitial cells were within the mass."

Rete Testis Adenoma and Adenocarcinoma

Gisser *et al.* (1977) reviewed the literature concerning adenocarcinoma of the rete testis in man and reported a case associated with asbestosis. Yoshitomi and Morii (1984) found 21 adenocarcinomas of the rete testis in man documented in the literature.

Newbold *et al.* (1985) reported the occurrence of "lesions resembling adenocarcinoma" of the rete testis in 11 of 233 mice that had been treated prenatally with diethylstilbestrol (DES). Comparable lesions were not seen in 96 age-matched control male mice. They concluded that "These results suggest an association of prenatal DES exposure and the subsequent development of testicular lesions in the rete testis of mice."

Searson (1980) reported a testicular adenocarcinoma in a ram and suggested that it probably originated in the rete testis. The neoplasm weighed 1550 g and completely replaced the right testis. It was gray-yellow, firm, and lobulated. The lobules consisted of solid and cystic tissue. Histologically, the neoplasm consisted of "numerous papillary projections, branching cords, and cystic spaces in an irregular pattern. These structures were lined by one to three layers of small cuboidal to low columnar epithelial cells with large spherical nuclei, one or two nucleoli, and pale cytoplasm . . . [and] mitotic figures were rare. The septa consisted of mature fibrous tissue" (Searson, 1980). Metastatic lesions were not found in lymph nodes, liver, kidney, spleen, or lung.

I have seen two equine and four canine neoplasms of the rete testis. One of the equine tumors was found during the routine examination of tissue sections of a retained testis from a 6-year-old Quarter Horse. The left testis weighed 292 g and the right 33.7 g. The left testis had focal areas of degeneration, which are present in most equine testes; otherwise it appeared normal. The seminiferous tubules in the right testis were lined merely by sustentacular cells. A small neoplasm of the rete testis was observed on microscopic examination. Some of the rete tubules were distended by papillary masses of cell with uniform-sized nuclei and rather scant cytoplasm (Fig. 15.18). No mitotic figures were evident. There was cystic distention of a number of the adjacent rete passages. The neoplasm was considered to be a rete adenoma.

A malignant equine tumor of the efferent ducts, possibly of rete origin, was submitted by Dr. K. W. Prasse of the College of Veterinary Medicine, Athens, Georgia. The tumor occurred in a retained testis of a 5-year-old Quarter Horse Palamino crossbred. The scrotal testis had been removed previously and the horse continued to act like a stallion. Therefore the retained testis was removed. It measured about 10 × 30 cm and contained irregular cavities filled with brown fluid. The major portion of the enlarged testis was neoplastic and consisted of solid masses and tubular structures lined by single to multilayered, cuboidal to columnar cells with numerous mitotic figures. Large areas of necrosis, mineralization, and hemorrhage were scattered throughout the neoplasm.

I have examined four unilateral neoplasms of the collecting system of the canine testis. One tumor appeared to be benign and the others malignant. The benign neoplasm was a 2-mm nodule of tubular tissue located in the caudal extremity of the testis of a 10-year-old Shetland sheepdog. The tumor consisted of anastomosing tubules lined by cuboidal cells with scant cytoplasm. Clusters of hemosiderin-laden macrophages were present in the lumina of many of the tubules. Blood vessels and a modest amount of collagenous connective tissue were dispersed among the tubules. The dog also had interstitial cell tumors, a seminoma, and a sustentacular cell tumor.

Malignant tumors of the rete testis were found in a 3-year-old mongrel dog, an aged German Shepherd, and an aged dog of unspecified breed. The neoplasms in two of the dogs occurred in retained testes. The 3-year-old, cryptorchid dog had a 3 × 4-mm neoplastic nodule in the central part of the caudal pole of one testis. The tumor consisted of solid cords and cystic tubules lined by epithelial cells with scant cytoplasm and oval to elongated hyperchromatic nuclei (Fig. 15.19). There was moderate mitotic activity. The neoplastic cords, with a moderate amount of connective tissue stroma, extended into the adjoining testicular tissue.

The tumor in an aged German Shepherd dog had replaced most of the testis and extended into the testicular capsule. The major portion of the tumor consisted of neoplastic cells in tubular arrangement with a minimal amount of supporting connective tissue. A few mitotic figures were present and many of the dividing cells were degenerating. Structures resembling rete tubules were located on the periphery of the neoplasm. These tubules blended with the less differentiated portion of the neoplasm.

The neoplasm in the other aged dog was about 5 × 7 cm in diameter and was located in the center of the testis. The neoplastic cells were arranged in tubules with prominent lumina in many areas. Several areas of transition from neoplastic tubules to normal tubuli recti were evident. Cells similar to those in the neoplasm are present in the receptacles of the testis and in the rete tubules of aged dogs.

Embryonal Carcinoma

Valentine and Weinstock (1986) reported an embryonal carcinoma of an enlarged right testis that was removed surgically from a 7-year-old Standardbred stallion. Enlarged sublumbar lymph nodes were palpated on per rectal examination 4 months later and the horse was killed. The affected testis measured 14 × 11 × 11 cm. The cut surface of the testis "was almost entirely replaced by a firm white lobulated mass with central necrosis and hemorrhage. . . . Pertinent

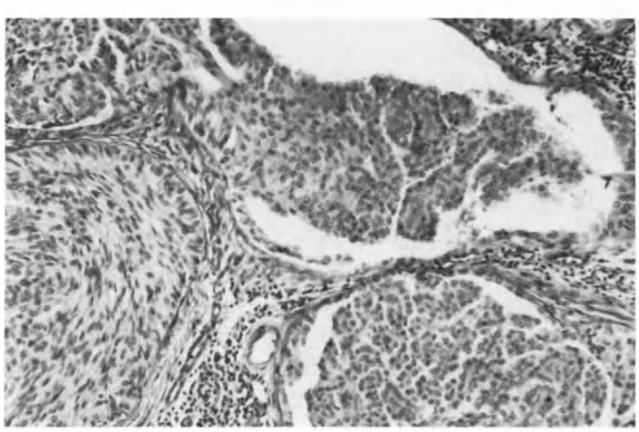

Fig. 15.18. Adenoma of rete testis from a 6-year-old Quarter Horse. ×178. Acc. No. 16449.

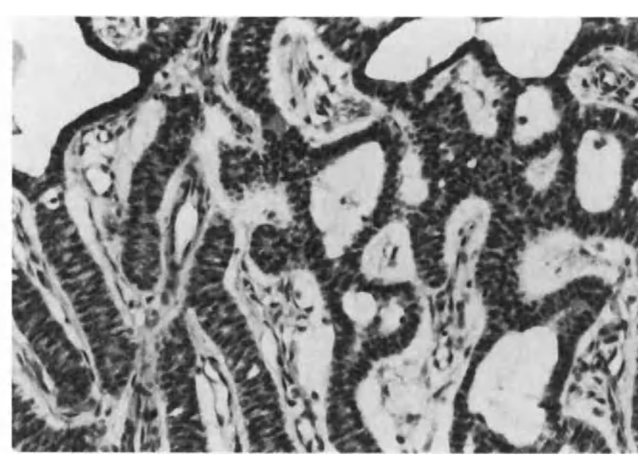

Fig. 15.19. Rete carcinoma in testis of a 3-year-old dog. ×178. Acc. No. 19608.

necropsy findings were multiple masses involving sublumbar and periaortic lymph nodes, parietal pleura, mediastinum, lung, and heart" (Valentine and Weinstock, 1986).

The testicular tumor consisted of multilobular masses of neoplastic cells separated by thick connective tissue septa. "The cell pattern varied from sheets and densely packed nests of cells to poorly differentiated acinar and tubular structures in abundant loose mesenchymal tissue stroma. Acini and tubules were lined by one to three layers of cells. The cells were pleomorphic, large round to cuboidal cells with large round vesicular nuclei, one to seven prominent nucleoli, and with a moderate amount of finely vacuolated pale basophilic cytoplasm" (Valentine and Weinstock, 1986). The cell boundaries were indistinct and numerous mitotic figures were present. There were areas of necrosis and hemorrhage with foci of bone in the necrotic tissue. The histologic appearance of the metastatic lesions was similar to that of the testicular tumor. Alpha-fetoprotein was demonstrated in the primary tumor but not in the metastases. They concluded that the histologic and ultrastructural appearance of the neoplasm and the presence of alpha-fetoprotein in the primary tumor fulfilled the criteria for a diagnosis of embryonal carcinoma. Although the authors dismissed the idea that the neoplasm might be a carcinoma of the rete testis, it has some features of this neoplasm.

Adrenal Rest Tumors of the Testis

Adrenal rest tumors of the testis have been reported in man but not in domestic mammals. Burke *et al.* (1973) stated that "Most of the 30 documented cases have been found at autopsy in patients with adrenogenital syndrome secondary to adrenocortical hyperplasia. In 14 cases the testes were noted to be enlarged or nodular. Although steroid therapy has been advocated for the treatment of these tumors, there are only seven reported cases of successful treatment." A major diagnostic problem is to differentiate these tumors from interstitial cell neoplasms. Most interstitial cell tumors in man are unilateral, whereas most adrenal rest tumors are bilateral. "The best means of differentiating these tumors is observation of response to treatment with exogenous steroids. While most cases have been found at autopsy, there are 8 reported cases, including the present one, in which these tumors regressed either clinically or histologically following steroid therapy" (Burke *et al.*, 1973). Not all patients respond to steroid therapy.

If adrenal rest tumors are to be found in domestic mammals, it would seem that they would be found in the stallion because of the frequent occurrence of accessory adrenal cortical tissue in and around the testes. I have examined the testes of many young but few old stallions without finding one of these neoplasms. Perhaps they will be found in old horses, which have a higher incidence of neoplasms of the adrenal cortex.

Secondary Carcinoma of the Testis

Price and Mostofi (1957) reviewed the cases of secondary carcinoma of the human testis in the collection at the Armed Forces Institute of Pathology. They stated that only 38 proven cases of secondary carcinoma were diagnosed. The collection of testicular neoplasms included more than 1600 primary testicular tumors. The main metastatic neoplasms included bronchogenic and prostatic carcinomas. The other metastases included carcinomas of the stomach, kidney, colon, pancreas, bladder, and rectum. They stated that "When a testicular carcinoma is secondary, it is usually found incidentally at autopsy of a patient with widespread metastatic disease, or at orchiectomy for prostatic carcinoma. . . . Occasionally, a secondary carcinoma becomes large enough to stimulate a primary testicular tumor" (Price and Mostofi, 1957).

Meares and Ho (1973) reported than fewer than 150 metastatic carcinomas of the testis were reported in man and that the most frequent primary site was the prostate gland. They stated that "Although the diagnosis is usually made at autopsy, occasionally the secondary testicular tumor has presented clinically and mimicked a primary testicular neoplasm. The peak incidence is during the sixth decade of life."

Secondary carcinomas of the testis appear to be rare in domestic mammals. This may be due to the relatively low incidence of prostatic carcinomas and to the failure to carefully examine testicular tissue in cases of carcinomas of other organs.

Teratoma

Testicular teratomas occur most frequently in the horse and rarely in other species of domestic mammals. According to Cotchin (1977b), "Silbersiepe and Meyer (1936) found one 'dermoid cyst,' in the course of operating on 140 cryptorchid horses, and Bishop *et al.* (1966) found one teratoma in 108 cryptorchid horses. A higher incidence was reported by Wright (1963), who found five teratomas in 50 abdominal testes."

Schlegel (1924) described a teratoma that occurred in a calf. Steiner and Bengston (1951) reported that a few cases of testicular teratomas have been reported in the boar. Machado *et al.* (1964) reported testicular teratomas in two dogs, but the lesions were not described.

I have examined a dermoid cyst from a dog. A firm, 8-mm nodule was found, as an incidental lesion, adjacent to the surface of the testis near the head of the epididymis in an adult Doberman Pinscher. The cyst was lined by stratified squamous epithelium and the center consisted of keratinized cells.

Gilbaugh *et al.* (1967) reported that in man, "epidermoid cysts of the testis are so rare that they constitute clinical and pathologic curiosities. . . . Only 27 cases of testicular epidermoids by 18 authors have been documented in the literature." Gilbaugh *et al.* described an additional three cases. They stated that "the epidermoid differs from the dermoid cyst in that the former lacks cutaneous adnexal structures such as hair follicles, sebaceous glands and sweat glands in the cysts." The epidermoid cyst is lined by stratified squamous epithelium that rests on connective tissue. The surrounding seminiferous tubules are compressed and atrophic and the remaining testicular tissue is normal. About 70% of the reported human cases were located in the center of the testis and the rest adjacent to the tunic.

Price (1969) examined 69 epidermoid cysts of the human testis. The cases which he classified as epidermoid cysts met the following criteria: "1) the lesion was a cyst located within the parenchyma of the testis, 2) the lumen of the cyst contained keratinized debris or amorphous material with cleft-like spaces, 3) the wall of the cyst was composed of fibrous tissue with a complete or incomplete inner lining of squamous epithelium and 4) no teratomatous elements or adnexal structures such as sebaceous glands or hair follicles were present either within the cyst wall or within the parenchyma of the testis."

Equine testicular teratomas are diagnosed mainly in 1- to 2-year-old horses and the majority occur in cryptorchid testes. (Willis, 1938; Willis & Rudduck, 1943). Ten of 13 equine teratomas that I have examined were present in retained testes. The location of the neoplastic gonads was not recorded for two of my cases. The occurrence of these tumors in young horses supports the theory that the neoplasms may be congenital. A large series of equine fetal testes should be examined to determine if this is so.

Stevens (1962) reported the occurrence of testicular teratomas in fetal mice. He stated that "The incidence of tumors in fetuses is the same as in older mice, which demonstrates origin during a prenatal period and not later. . . . All 24 tumorous foci in testes of 15- and 16-day fetuses were entirely enclosed within intact seminiferous tubules, which demonstrated that they were derived from a component of the seminiferous tubules, probably the primordial germ cell." Teratomas extended beyond the seminiferous tubules in older fetuses.

No particular equine breed appears to be especially prone to develop these neoplasms. Cotchin (1977b) mentioned that a number of breeds of draft horses, light horses, and ponies were affected. In my series of 13 cases, the breed was not recorded for four animals. The rest consisted of two Quarter Horses, two Clydesdales, two Arabians, one Thoroughbred, one Appaloosa, and one Belgian.

Testicular teratomas are usually cystic and occasionally solid neoplasms (Figs. 15.20, 15.21, and 15.22). One or more large cysts are frequently evident and may comprise a large portion of the tumor. A number of tissue sections should be prepared so that all the tissues that are present can be identified. A variety of tissues are frequently overlooked when only one or two tissue sections are examined. Cotchin remarked that nerve tissue was present in all 16 of his cases and adipose tissue was usually present. Other tissues may include glandular elements, hair and adnexal structures, fibrous tissue, cartilage, bone, teeth, and choroid plexus. Liver, kidney, and spleen are rarely present . The presence of testis or ovary has not been reported.

Malignant Lymphoma

Mostofi (1973) stated that the malignant lymphoma is the most important metastatic tumor of the testis in man. Paladugu *et al.* (1980) reported 38 cases of malignant lymphoma in which the gonad was the site of the main tumor at the time of diagnosis in 27 men and 11 women.

Givler (1969) stated that "Microscopic testicular infiltration was found at autopsy in 64.3 percent of 140 males with acute leukemia, 22.4 percent of 76 males with chronic leukemia, 18.6 percent of 102 males with lymphosarcoma, and in none of 44 males with Hodgkin's disease. . . . In both leukemia and lymph-

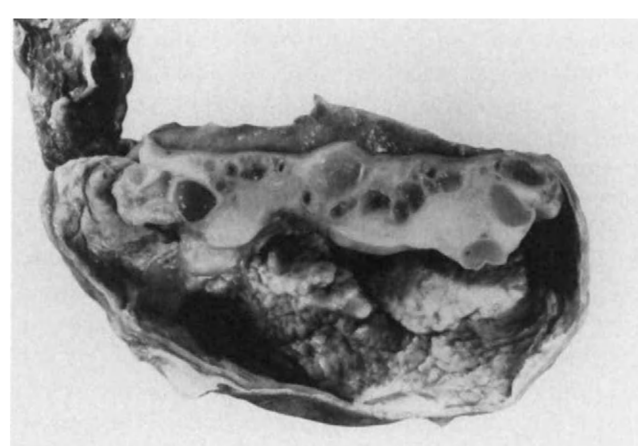

Fig. 15.20. Cystic teratoma in an abdominal testis of a 19-month-old Quarter Horse. Acc. No. 14793.

Fig. 15.21. Teratoma in caudal part of testis from a 4-year-old Belgian stallion. Acc. No. 9109.

oma, testicular involvement at autopsy was usually associated with widespread and extensive infiltration elsewhere."

I have seen malignant lymphoma in the testes of the dog (Fig. 15.23) and the bull, but the incidence of these tumors in the testes of domestic mammals has not been established. Testes are not examined carefully in most animals with widespread lymphomas.

Mesothelioma

I have seen one mesothelioma of the spermatic cord in a dog and three involving the testicular tunics in bulls. All the lesions were unilateral. Two of the bovine tumors were metastases from peritoneal neoplasms in young animals, and the third was located

Fig. 15.22. Solid equine teratoma that weighed 627 g and completely replaced normal testicular tissue. Acc. No. 3857.

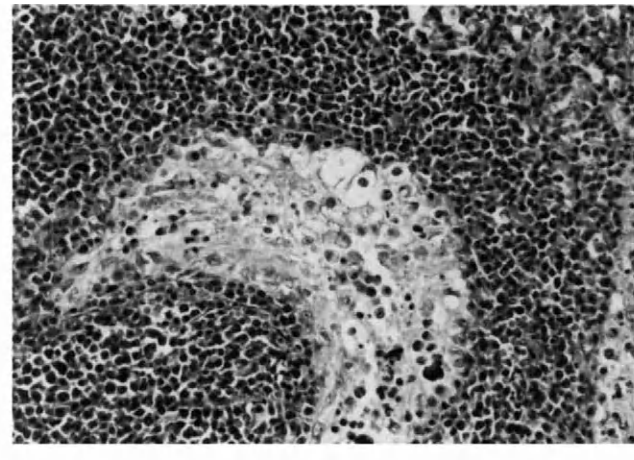

Fig. 15.23. Malignant lymphoma in testis of a dog. ×178. Acc. No. 18821.

in the testicular tunics of a 5 1/2-year-old Holstein-Friesian bull. The bull was submitted to surgery because of enlargement of the left scrotal contents. The left testis was removed surgically. Numerous soft red papillary growths covered the tunica vaginalis (Fig. 15.24). At the time of surgery, it was thought that the lesion had metastasized from the peritoneal cavity. However, no peritoneal tumors were found when the bull was killed 3 years and 7 months later.

Cotchin (1960b) reported a mesothelioma of the scrotum in a 1-month-old calf. Ladds and Crane

Fig. 15.24. Mesothelioma of testicular tunics in a bull. Acc. No. 12513.

(1976) described a scrotal mesothelioma from a mature bull with testicular degeneration.

Cihak *et al.* (1986) reported a malignant mesothelioma of the right tunica vaginalis of a 12-year-old Scottish Terrier dog. The neoplasm, testis, and epididymis were removed surgically. The dog became weak and developed abdominal distention within a few weeks and died 3 months after surgery. Abundant ascitic fluid was present in the abdominal cavity and numerous small tumor nodules were present on the peritoneum.

Tumors of the Appendix Testis

Sundarasivarao (1953) and Bailey *et al.* (1955) reported epithelial tumors that appeared to develop from the appendix testis in man. Although I have not seen a neoplasm of the appendix testis in domestic mammals, I believe that they should occur, especially in the horse. All the equine testes that I have examined contained an appendix testis. The vestigial structure is occasionally present in other species of domestic mammals with the exception of the bull. The majority of equine testes that I have examined were from comparatively young animals, and I would expect the tumor to develop in old stallions.

Hemangioma

There are very few reports of hemangiomas of the testis in domestic mammals. I have examined two in dogs, one of which was a metastatic neoplasm. Fisher and Olander (1978) reported a large testicular hemangiosarcoma in a 5-year-old Yorkshire boar. The tumor weighed 7 kg and measured 28 × 18 cm. They stated that the tumor "was composed of a tight network of plump, pleomorphic spindle cells, often enclosing blood-filled spaces. The mitotic index was moderately high."

Clarke (1979) reported a testicular hemangiosarcoma in an abdominal testis of a 9-year-old Boxer that was presented for treatment of a perineal hernia. "On exploration of the abdomen a grossly enlarged and discolored left testis, approximately 15 cm in diameter, was found." A portion of omentum and the spleen were attached to the testis. The spleen and attached omentum were removed with the enlarged, dark red testis. The testicular tumor was diagnosed as a hemangiosarcoma on the basis of histologic examination. The dog was apparently normal 18 months following surgery.

Leiomyoma

I have seen only one leiomyoma of the testicular tunic and that was a small incidental finding in an 11-year-old Beagle. Patnaik and Liu (1975) reported a case in a 13-year-old Miniature Poodle. The neoplasm had caused hydrocele and atrophy of the ipsilateral testis. Klug *et al.* (1972) reported bilateral leiomyomas of the testicular tunics in an 18-year-old stallion.

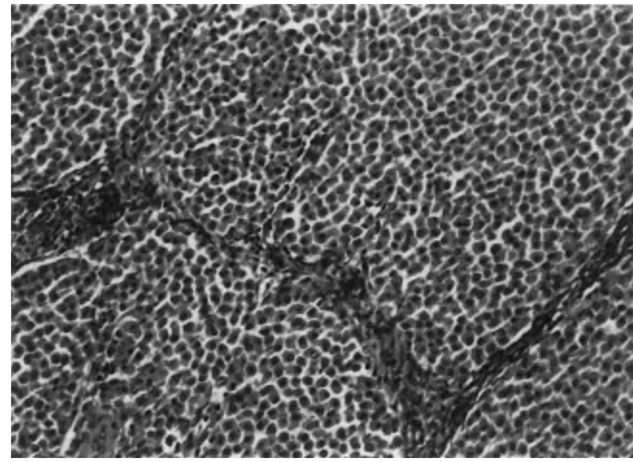

Fig. 15.25. Testicular mastocytoma from a 20-year-old stallion. ×178. Acc. No. 15606.

Mast Cell Tumor (Mastocytoma)

I examined a mast cell tumor of the left testis from a 20-year-old Arabian stallion. It is the only testicular tumor of this type that I have seen, and I am not aware of any other reported cases. The lesion was found at necropsy in a stallion that had died of an intestinal rupture. The testis measured 8.5 × 5.5 cm and the neoplasm occupied about 2.5 cm of the testis adjacent to the attached border.

The neoplastic cells were arranged in irregular-shaped clusters separated by thin bands of spindle-shaped cells (Figs. 15.25 and 25.26) containing gran-

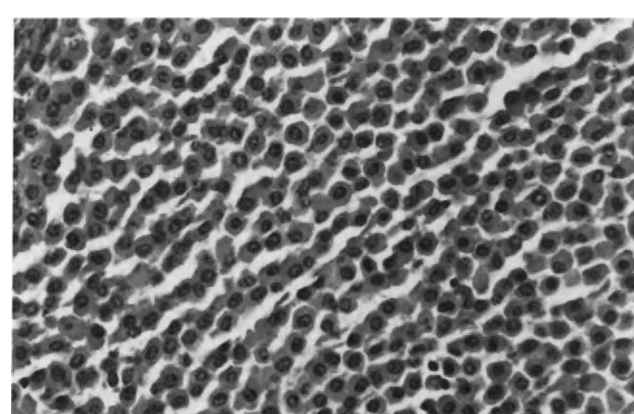

Fig. 15.26. Testicular mastocytoma from a stallion. ×385. Acc. No. 15606.

ules of brown pigment. Broad fingerlike masses of tumor cells extended into the adjacent testicular tissue, which appeared normal. The tumor cells were polyhedral and contained abundant eosinophilic cytoplasm. The nuclei were oval to spherical and quite uniform in size. Giemsa staining revealed cytoplasmic granules in the tumor cells. The pigment in the stroma of the tumor appeared to be hemosiderin.

Schwannoma

Rothwell *et al.* (1986) reported a schwannoma of the right testis from an 11-year-old dog. The parenchyma of the testis consisted of a "firm, pale brown, finely lobulated tumor which bulged slightly from the cut surface. . . . The tumor was composed of interwoven bundles or whorls of fusiform cells." The authors concluded on the basis of electron microscopy and immunocytochemical examination that the neoplasm was a schwannoma and not a smooth muscle tumor.

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Chapter 16

Efferent Ductules, Epididymis, and Deferent Duct

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- Epididymis (Ductus Epididymidis)
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- Ectopic Adrenocortical Tissue
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Bibliography

The ducts outside of the testis in domestic mammals include the extratesticular rete testis, efferent ductules, epididymis, and deferent duct. Only a small portion of the rete testis extends beyond the testicular capsule to join the efferent ductules. The efferent ductules and the epididymis proper constitute the organ known as the epididymis.

Anatomic Features

Efferent Ductules (Ductuli Efferentes)

The portion of the head of the epididymis of domestic mammals that contains the efferent ductules can be identified on gross examination of tissue from mature animals because of the presence of a pale gray-green to brown pigment. The pigment accumulates in the epithelium and the surrounding connective tissue of the efferent ductules as a result of phagocytosis of spermatozoa.

Mitchinson *et al.* (1975) reported the occurrence of "brown patches" in the area of efferent ductules in 66 out of 100 consecutive human necropsies. They stated that the "pigment was negative to stains for iron and melanin, and stained positively with PAS and with Sudan III and IV even in paraffin wax-embedded sections. This suggested that it was similar to lipofuscin." The pigment was found within the cytoplasm of the efferent ductule epithelium and within macrophages in adjacent comnective tissue. They concluded that "the presence of brown pigment in the macrophages seems to be due to the phagocytosis and partial degradation of spermatozoa in the lumen."

The efferent ductule area of the equine epididymis appears to be edematous because a gelatinous material is present in the intertubular connective tissue.

Mobilio and Campus (1912–1913), Ghetie (1939), and Hemeida *et al.* (1978) studied the anatomy of the efferent ductules in domestic mammals. The latter authors reported that on the basis of their findings and "the data of others relating them to the total number of specimens examined in each species, an estimate (narrow range) was made of the minimal–maximal numbers of efferent ductules as follows: dog 13 to 15; cat 14 to 17; boar 14 to 16; goat 18 to 19; ram 17 to 20; bull 13 to 16; and stallion 14 to 17" (Hemeida *et al.*, 1978). According to Hemeida *et al.*, the minimal–maximal numbers of efferent ductules reported by various authors are: dog, 13–16; cat, 13–18; boar, 8–21; goat, 16–19; ram, 15–25; bull, 10–20; and stallion, 10–23. The number of epididymides examined included: dog, 7; cat, 14; boar, 6; goat, 8; ram, 8; bull, 34; and stallion, 45.

Individual efferent ductules consist of three segments: a nearly straight part that leaves the rete testis; a long, highly convoluted central section; and a moderately convoluted terminal segment that enters the epididymis (Fig. 16.1). The luminal diameter of the efferent ductules decreases markedly in the terminal segment. Two or more efferent ductules frequently join a common terminal segment before entering the epididymal lumen (Fig. 16.2). Hemeida *et al.* (1978) found two anatomic patterns of efferent ductules in the horse. In about 75% of the specimens the ductules entered the epididymis at various levels, whereas in about 25% of the specimens several ductules joined to form common ductules and these entered the epididymis at its proximal part. The rete tubules, efferent ductules, and epididymal duct can be differentiated easily on histologic examination by the marked differences in the epithelial height. The epithelium of the efferent ductules is taller than that of the rete testis but not as tall as that of the epididymal duct.

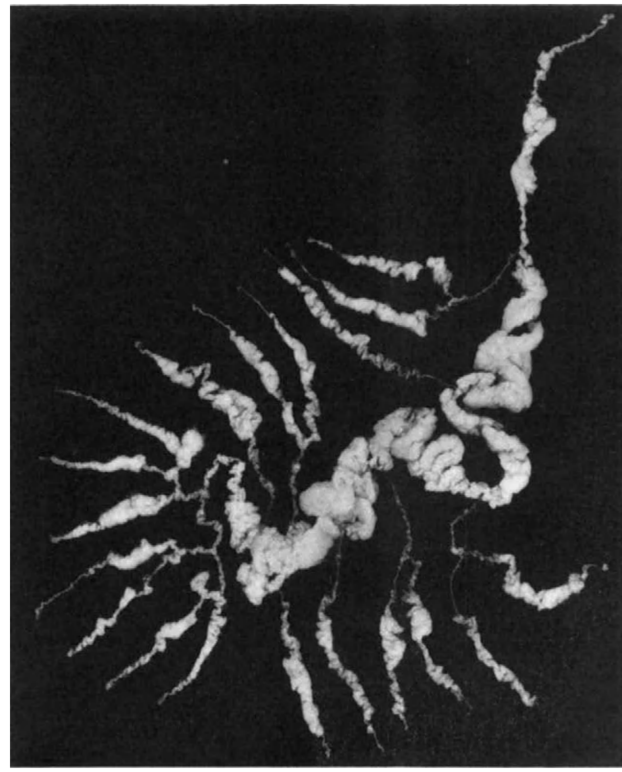

Fig. 16.2. Dissected efferent ductules from a goat. Many of the ductules join a common duct before entering the epididymis. Acc. No. 15717. (From Hemeida *et al.*, 1978.)

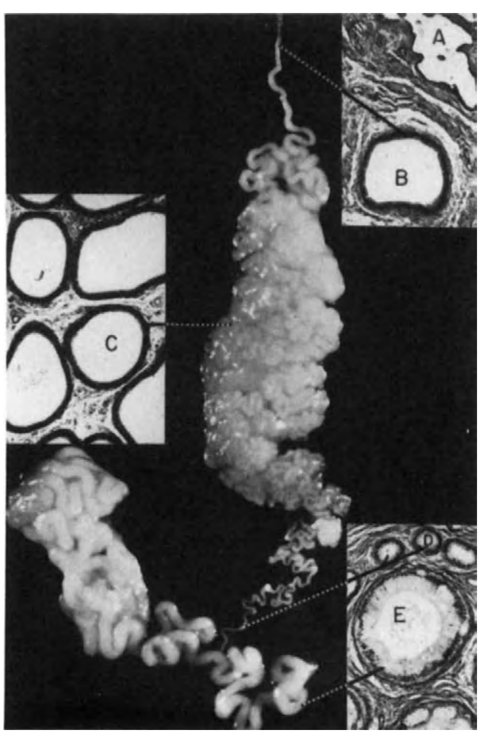

Fig. 16.1. Composite of a portion of a bovine rete tubule (A), epididymis (E), and an efferent ductule with cross sections, at the same magnification, of the nearly straight initial segment B, the highly convoluted middle section C, and the moderately convoluted terminal section D. Acc. No. 18249. (From Hemeida *et al.*, 1978.)

The epithelium of the efferent ductules consists of ciliated and nonciliated cells. The nonciliated cells are classified into three types: type I cells contain neither granules nor vacuoles, type II cells have cytoplasmic granules, and type III cells contain cytoplasmic vacuoles. Goyal and Hrudka (1981) studied the efferent ductules of the bull and reported that "The specific granules of type II cells stain with eosin, Toluidine blue, periodic acid–Schiff and osmium but are negative after acid phosphatase, Alcian blue and Sudan black staining. These data suggest that the content of granules is a glycoprotein." The granules increase in size from the basal to luminal pole of the type II cells and they disappear after orchidectomy.

"The vacuoles of type III cells do not stain with eosin, Toluidine blue, osmium or periodic acid–Schiff, nor with acid phosphatase, Sudan black or Alcian blue techniques. The small flocculent and membranous content of the vacuoles, which is found especially after glutaraldehyde perfusion, may indicate a low density of phospholipids" (Goyal and Hrudka, 1981). Vacuoles are present in the subnuclear half of the cells but these disappear after orchidectomy. Goyal and Hrudka (1981) reported that the granule-producing cells occur in the proximal segment and cells producing vacuoles are present in the distal segment of the efferent ductule. They found that the first appearance of granules precedes that of the vacuoles by several weeks, that granules do not convert to vacuoles and vice versa, and that the content of granules and vacuoles differs in histochemical and physical properties. They suggested that the granules may play an important role in sperm maturation. "A concomitant onset of production of specific granules and spermatozoa lends support to the above hypothesis. There is some evidence that specific granules are of significance in producing sperm antigens or sperm coating protein. Since the granules contain glycoprotein, one can assume that they may be a source of nutrients and/or of other factors necessary for priming sperm motility, which is believed to be initiated in this segment" (Goyal and Hrudka, 1981). The role of vacuoles is unknown.

Epididymis (Ductus Epididymidis)

The word epididymis is derived from the Greek words *epi* (upon) and *didymos* (twin). Since the testes are alike (twins), the structures that cover part of the testes are called epididymides. The epididymis consists of a single very tortuous duct that is 40 to 50 m long in the bull and 62–64 m in the boar (Ghetie, 1939). According to Martin and Schauder (1938), the epididymal duct of the bull is 33 to 35 m long. The principal segments of the epididymis are the head (caput, initial segment), body (corpus, middle segment), and tail (cauda, terminal segment). The location of the epididymis, in relation to the body wall, varies among the different species of domestic mammals. The tail of the epididymis is ventral in the bull, ram, and goat; caudal in the stallion; and caudodorsal in the dog, cat, and boar.

Bull. Blom and Christensen (1947) stated that the "Caput epididymis (of the bull) forms a flattened, somewhat cup-shaped, protrusion, varying somewhat in outline and size, on the lateral aspect of the cranioproximal surface of the testis. Usually it is U-formed, and the tip of the bend may extend one third down on the cranial aspect of the testis." The initial portion of the corpus epididymis in some calves loops proximally along the spermatic cord. As the testis develops this epididymal loop is usually pulled down to the testis. Blom and Christensen (1956a) referred to the condition as a high epididymal loop. The corpus epididymis continues ventrally, as a comparatively narrow structure, along the caudomedial side of the gonad. The cauda epididymis is relatively large when it is filled with spermatozoa. It is reduced markedly in size when it is empty as in the case of obstruction of the epididymal lumen at a higher level. Blom and Christensen (1956a) reported that "The cauda may vary somewhat in form and be more or less closely connected with the testis, making a U-formed loop round the ligamentum testis, which is the proximal remnant of the connective tissue cord (gubernaculum Hunteri), which during development contributes to bring the testis from the lumbar region down into the scrotum."

Amann and Almquist (1962a) studied the effect of unilateral vasectomy and ejaculation frequency on sperm reserves in nine 36-month-old Holstein bulls that were kept for 23 weeks following vasectomy. The bulls were divided into three groups subjected to the following regimen: sexual rest, two ejaculates per week, and eight ejaculates per week for the last 20 weeks before slaughter. "The apparent rate of sperm resorption in the epididymis on the intact side of three bulls collected eight times weekly was 57%. In the vasectomized sides of nine bulls, it was greater than 96%. The rate of resorption was postulated to be dependent upon the number of spermatozoa present in the cauda epididymis" (Amann and Almquist, 1962a). Sperm reserves in the caput and corpus epididymis were not affected by vasectomy.

Stallion. The epididymis of the stallion is not as closely attached to the testis as it is in other species of domestic mammals. The cauda and corpus epididymis may descend into the scrotum while the caput epididymis and testis are retained in the abdomen (Williams, 1909). Thus an inexperienced surgeon may remove the epididymal tail and leave its body and head and the testis in the abdominal cavity. Major surgery is required to remove the testis and the remainder of the epididymis. I know of one case in which only a portion of the epididymal body was removed during the second operation and the testis and head of the epididymis were still left in the abdominal cavity.

Dog and Cat. The epididymis of the dog and cat is of rather uniform size through its entire length. Intranuclear, eosinophilic, somewhat hyaline inclusion bodies that are Schiff positive are normal in the canine epididymis (Fig. 16.3) and should not be confused with distemper inclusions, which are Schiff negative. MacDonald (1950) described the cytochemical characteristics of these inclusions in man. He reported that "The inclusions are composed of a basic protein of the histone type and contain arginine, as demonstrated by the Sakoguchi reaction. Although the inclusions are acidophilic and do not exhibit metachromasia, they are Schiff positive and could possibly contain a protein–carbohydrate complex." I am not aware of the significance of the inclusions.

Histology. Nicander (1957) described the regional differences in the histology and cytochemistry of the

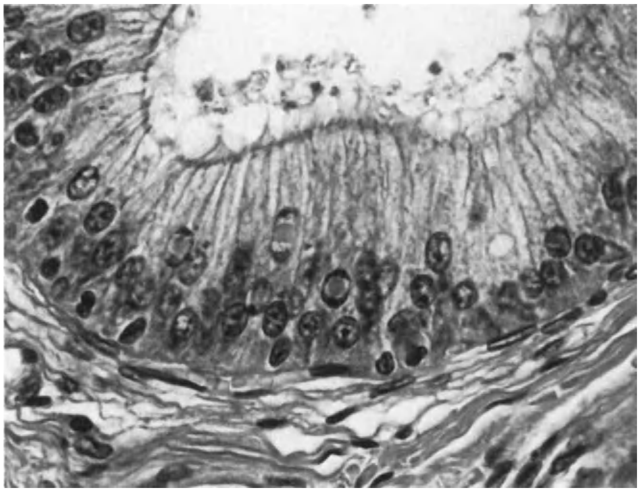

Fig. 16.3. Normal intranuclear inclusion bodies in the epididymis of a 10-year-old dog. ×370. Acc. No. 16450.

epithelium of the epididymal duct in the bull, ram, and stallion. He stated that "Regional differences in the ductus epididymis were detected long ago by Hammar (1897) in dogs. . . . Later investigations on the structure of the duct have not brought any noticeable new information on the subject, though there has been general agreement upon the correctness of Hammar's observations as regards dogs, and upon the observation that the epithelium is very high in the proximal part of the duct, moderately high in the intermediate parts, and low in the cauda, whereas the lumen is narrow at the beginning and widens continually throughout the organ."

Nicander described six different regions of the epididymis of the stallion, ram, and bull. The first region is adjacent to the efferent ductules. His descriptions are as follows:

Regions 1, 2, and 3 are in the head of the epididymis. Region 1 "shows a generally high but irregular epithelium, especially in bulls. Prominent Golgi apparatuses, with some faintly stainable granules and a strongly basophilic cytoplasm below them, characterize the columnar cells. Stallions often show large lipid inclusions near the apex of the highest cells" (Nicander, 1957). Spermatozoa are sparse in this region.

Region 2 has a lower epithelium with weaker basophilia. The nuclei are unusually small in bulls and the cytoplasmic basophilia is concentrated above the Golgi apparatus. A hyaline substance is present in the lumen in regions 2 and 3 in stallions.

Region 3 is characterized by "numerous unstable inclusions throughout the cytoplasm of all columnar cells."

Regions 4 and 5 comprise the body of the epididymis. Region 4 has a lower epithelium. "Characteristic granules are seen below the nuclei of the columnar cells. Moreover, numerous lipid droplets are generally present in stallions, and specific vacuoles in bulls and rams."

Region 5 is lined by somewhat taller epithelial cells than in region 4. This is in contrast to the previously held view that the epithelial cell height decreases throughout the length of the epididymis.

Region 6 comprises the tail of the epididymis, which has a large lumen and a lower epithelium than the rest of the epididymal duct. Densely packed spermatozoa are present in the lumen of normal mature animals. The muscle is much thicker than in the more proximal portions of the duct.

The functions of the epididymis are (1) to convey sperm from the efferent ductules to the ductus deferens, (2) to play a role in sperm maturation, (3) to store and nourish sperm, (4) to accomplish the dissolution of ageing sperm, and (5) to resorb fluids and products of sperm breakdown.

Deferent Duct (Ductus Deferens)

There is not a clear morphologic distinction between the terminal part of the epididymis and the beginning of the deferent duct. The terminal portion of the deferent ducts widen to form the ampullae of the deferent ducts in all domestic mammals except the cat and the boar.

Blom and Christensen (1947) reported the relative location of the ampullae to the vesicular glands in 55 normal Red Danish Milk Breed bulls. The ampullae were dorsal to the vesicular glands in 22 bulls, ventral in 21 bulls, and intermediate in 12 bulls.

Bagshaw and Ladds (1974b) reported the relationship of the ampullae to the vesicular glands in 162 bulls. The ampullae were dorsal to the vesicular glands in 77 bulls, intermediate in their relationship in 66 bulls, ventral to the vesicular glands in 10 bulls, and mixed in their relationship in 9 bulls. There was no correlation of duct relationships according to breed or age.

Congenital Anomalies

Melanosis of the Epididymis

Melanosis of the epididymis occurs frequently in the ram and occasionally in the bull. Blom and Christensen (1956a,b) reported melanosis of the epididymis in bulls. The incidence of pigmentation was higher in Red Danish Milk Breed calves than in Jersey calves and appeared to decrease with increasing age.

Ladds *et al.* (1973) found melanosis of the epididymis in 21 (3.8%) of 550 slaughtered beef bulls from Queensland and the Northern Territory in Australia. The pigmentation was unilateral in 17 bulls and bilateral in 4; it involved the body of the epididymis in 13 bulls, the tail in 7, and the head in 1 bull.

Ectopic Adrenocortical Tissue

Widmaier (1959) reported the presence in goats of adrenocortical tissue in the head of the epididymis between the pampiniform plexus and the efferent ductules. The adrenal inclusions were found in 3 of 16 intersexes, in 6 of 27 hornless goats, and in 1 of 8 horned goats.

I have found that adrenocortical rests occur frequently in the epididymis, testis, and lower portion of the spermatic cord in the horse and occasionally in other species of domestic mammals. Blom and Christensen (1958) reported the presence of ectopic adrenocortical tissue, associated with the head of the epididymis, in two bulls.

Cysts of the Appendix Epididymis

The appendix of the epididymis is a remnant of the proximal end of the mesonephric duct. Cysts of this structure occur occasionally in all species of domestic mammals. They are usually located between the head of the epididymis and the testis (Figs. 16.4 and 16.5) but occasionally occur on the surface of the testis adjacent to the epididymis. Although the cysts that are located under the epididymal head may be several centimeters in diameter, they do not interfere with the passage of sperm. The cysts enlarge very slowly over a long period of time and the lumen of the epididymal duct is not compressed.

Watt (1971) reported the occurrence of cysts on the head of the epididymis in 136 (5.96%) of 2281 Merino rams slaughtered at an abattoir in Western Australia. The cysts were unilateral in 80 rams and bilateral in 56. He stated that the cysts "were observed in the anterior aspect of the head of the epididymis, near its ventral border, as slightly raised, focal, circular, cystic structures 1 to 4 mm in diameter."

Fig. 16.4. Cystic appendix epididymis located between the head of the epididymis and the testis of a boar. Acc. No. 5637.

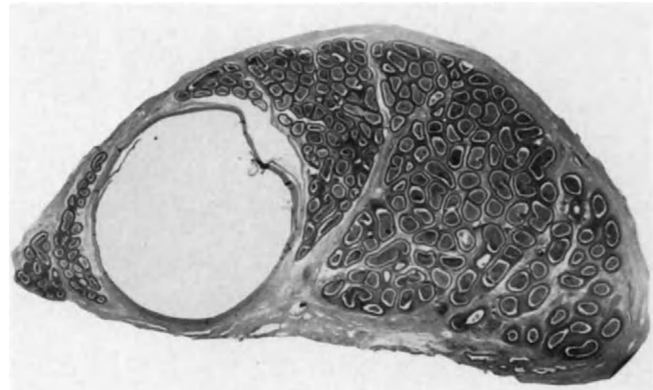

Fig. 16.5. Cystic appendix epididymis in the head of the epididymis of a bull. ×3. Acc. No. 10585.

Uterus Masculinus

The term uterus masculinus refers to the remnants of the paramesonephric ducts in the male. Blom and Christensen (1958) reported that "according to the investigations reported by Skoda (1917) and later confirmed by Swoboda (1929), these rudiments are preserved in the bull far more frequently than generally assumed, being found in respectively 71% and 50% of the bulls examined. Most often the remnants consisted merely of a single, rather firm vesicle (less frequently 2 or 3) of about pea size, filled with mucus, situated in the anterior part of the plica urogenitalis."

Bagshaw and Ladds (1974b) found cysts in the urogenital fold of 34 (6.5%) of 521 slaughtered bulls in Australia. "Cysts varied in size from 0.1 to 2 cm in diameter and 4 cm in length. Breed incidence was 18% in Brahmans, 11% in Brahman-cross and 4% in bulls of British breed. The cysts contained a clear gelatinous fluid and were surrounded by a thick fibrous and muscular capsule; the epithelial lining was folded to resemble immature uterus."

Blind-Ending Efferent Ductules

Blind-ending efferent ductules (Fig. 16.6) occur frequently in domestic mammals. Hemeida *et al.* (1978) found them in "1 of 2 porcine, 1 of 6 caprine, 2 of 5 ovine, 8 of 25 bovine, and 13 of 19 equine epididymides examined. The numbers of blind-ending ductules per affected male were 4 in the boar, 1 in the goat, 2 to 3 in the ram, 1 to 5 in the bull, and 1 to 14

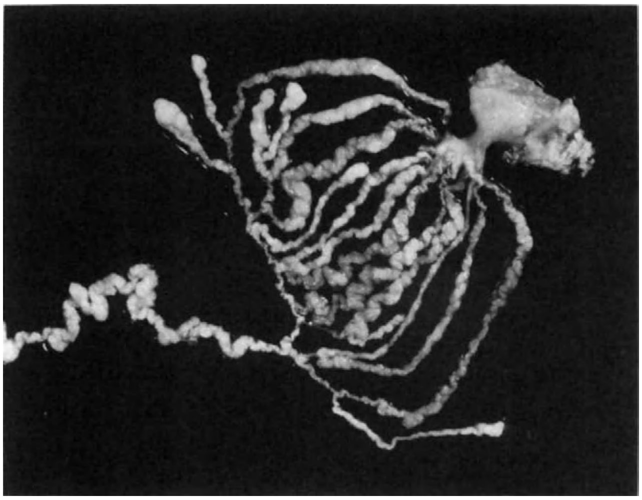

Fig. 16.6. Equine efferent ductules with seven blind-ending ductules. Acc. No. 15800. (Dissected by Dr. Nabil Hemeida.)

in the stallion. From our work, it appears that in the bull and stallion at least, blind-ending ductules were present in sufficient numbers to be considered a factor in spermiostasis and the infertility resulting from it."

More dissections of efferent ductules need to be conducted on all species of animals and especially on polled goats, which have a high incidence of sperm granulomas in the head of the epididymis. Most of these granulomas are probably secondary to sperm stasis in blind-ending efferent ductules. The dissections need to be conducted on young animals before large sperm granulomas develop and destroy many of the tubules.

Failure of the Efferent Ductules to Join the Epididymis

Figure 16.7 illustrates a congenital malformation of the right epididymis of a 2-year-old Holstein-Friesian bull. There was a failure of all the efferent ductules to join the epididymis, which remained small. Histologic examination revealed the presence of a lumen in all segments of the epididymis. A sperm granuloma caused enlargement of the area of the efferent ductules.

Aplasia of the Efferent Ductules

Hemeida *et al.* (1978) reported bilateral aplasia of the efferent ductules in a Holstein-Friesian bull. They stated that "On the left, there was no connection between the testis and the epididymal duct except for a few short thin transparent strands of connective tissue. On the right, there were 5 hypoplastic ductules." I have likewise seen a case of aplasia of the efferent ductules in a Holstein-Friesian bull.

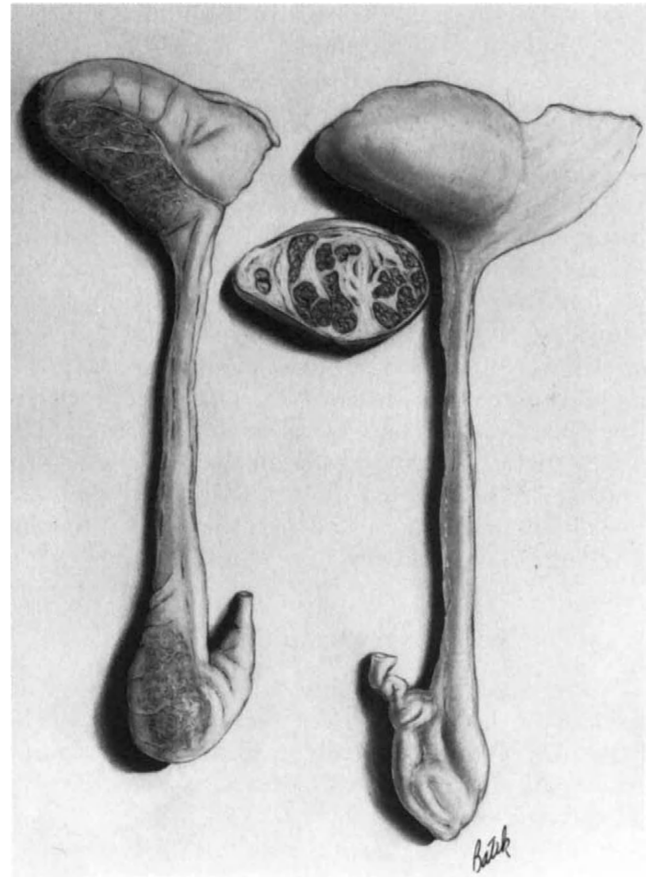

Fig. 16.7. Failure of the efferent ductules to join the right epididymis of a bull. Acc. No. 13820.

Blom (1982) reported a case of aplasia of the efferent ductules in a 15-month-old Holstein-Friesian bull with aspermia and swelling of both testes. The right testis and epididymis weighed 700 g and the left testis and epididymis weighed 600 g. Both testes were edematous. "The characteristic ductuli efferentes epithelium was only found in a group of rudimentary ducts, collapsed and empty, situated in the right caput epididymis. In the rete testis an accumulation of loose sperm heads and a strong spermiolphagic reaction were seen both in the epithelium and in the interstitia, characterized by abundant occurrence of giant cells and plasma cells" (Blom, 1982). The epididymides were present but devoid of spermatozoa.

Aplasia of the Epididymis

Bull. Gilman and Hopper (1925) reported a case of segmental aplasia of the left epididymis and left vesicular gland of a Guernsey bull. The head and body of the epididymis were underdeveloped and the epididymal tail was represented by a small elongated structure. The left vesicular gland was small, had a smooth surface, and a central cavity filled with mucus.

Blom and Christensen (1947) conducted clinical examinations on 2000 bulls, the majority of which were of the Red Danish Milk Breed. The reproductive organs were examined following slaughter from most of the bulls with clinically diagnosed reproductive lesions. Aplasia of the epididymis and/or ductus deferens was found in seven bulls of the Red Danish Milk Breed. The lesions occurred on the right side in six bulls and on the left side in one bull. Aplasia of the vesicular gland was diagnosed in four bulls and it occurred on the side with the affected epididymis.

Blom and Christensen (1951) reviewed the cases of epididymal aplasia that were reported in 1947 and described four additional cases. Three of the new cases occurred in Red Danish Milk Breed bulls and one was found in a Jutlandic bull. The gross and microscopic lesions of the 11 cases were described in detail. The aplasia was bilateral in one bull, localized on the right side in eight bulls, and affected the left side in two bulls.

A twelfth Red Danish Milk Breed bull, with aplasia of the right epididymis, was slaughtered after the other 11 cases were described in detail. Nineteen of his sons, born of different cows, were examined clinically. Four had unilateral epididymal aplasia. The right epididymis was lacking in three bulls and the left epididymis and left vesicular gland were deficient in one bull.

Blom and Christensen (1956a) examined the reproductive organs of 38 adult bulls, 452 fattening male calves, and 4892 newborn bull calves. They reported that "segmental aplasia of the Wolffian duct was established in Zealand with a frequency of 1.15% in new-born calves and 1.18% in fattening calves. In Funen the frequency was 0.59% among RDM (Red Danish Milk Breed), while it was absent in the Jersey calves. The higher frequency in Zealand may partly be explained by the fact that one bull, itself suffering from the defect, accounts for a little less than one-third of the cases." Forty cases of segmental aplasia of the mesonephric duct were observed of which 29 were right-sided and 11 left-sided.

van der Sluis (1953) reported 41 cases (5%) of aplasia of the epididymis in 828 bulls in The Netherlands. The condition was bilateral in 14 animals. The breed(s) of affected bulls was not reported.

König *et al.* (1972) reported the occurrence of epididymal aplasia in 18 Simmental bulls. Both epididymides were affected in 12 bulls, 3 bulls had left-sided aplasia, and 3 had aplasia on the right side. They concluded, from the genealogical data, that in all probability an autosomal recessive gene was responsible for the condition.

I have examined the reproductive organs from 10 bulls with segmental aplasia of the epididymis: 1 Guernsey, 1 Aberdeen Angus, and 8 Holstein-Friesians. Most of the bulls were 1 to 2 years old when the condition was diagnosed and they were slaughtered. McEntee (1958) reported a case of segmental aplasia of the left epididymis, ductus deferens, and vesicular gland in a 10-year-old Guernsey bull that was used for artificial insemination until it had a low concentration of sperm. The poor semen quality was due to the presence of large, bilateral interstitial cell tumors. The left epididymis weighed only 8.5 g, whereas the right epididymis weighed 50.5 g. The left vesicular gland and left ampulla were cystic and failed to open into the urethra.

Goat. Humenhuk and Vinha (1976) reported three cases of segmental aplasia of the epididymis found during the examination of 100 slaughtered goats. One case was bilateral, one affected the left epididymis, and one the right epididymis.

Ram. Fraser and Penman (1971) reported unilateral aplasia of the epididymal tail in two rams and bilateral aplasia of the epididymis in one ram.

Dog. Majeed (1974) reported a case of segmental aplasia of the epididymis in a white Poodle dog. The tail and part of the body of the epididymis were missing on both sides. Copeland and Maclachlan (1976) described a case of aplasia of the epididymis and ductus deferens in a Golden Retriever dog. During exploratory surgery, aplasia was noticed in a portion of the epididymal body, in its tail, and in the deferent duct on the left side. The distal part of the right epididymal body and tail were distended with sperm, which suggests that the deferent duct had an area of aplasia even though this was not revealed during the examination. Spermatozoa were not found in three ejaculates collected over a period of 3 weeks.

Figure 16.8 illustrates a case of segmental aplasia of the body and tail of the left epididymis of a 1-year-old Boston Terrier dog. The lesion was an incidental finding during a necropsy.

Man. Kaplan *et al.* (1968) reported the occurrence of aplasia of the deferent duct and epididymis in young men with cystic fibrosis. They stated that "Of approximately 2300 patients with cystic fibrosis seen in our clinic over the past 28 years, 115 males had reached 17 years of age or over. . . . Fifteen married, and 12 of these are living. Only one offspring has been reported in these marriages."

Landing *et al.* (1969) conducted "microdissection

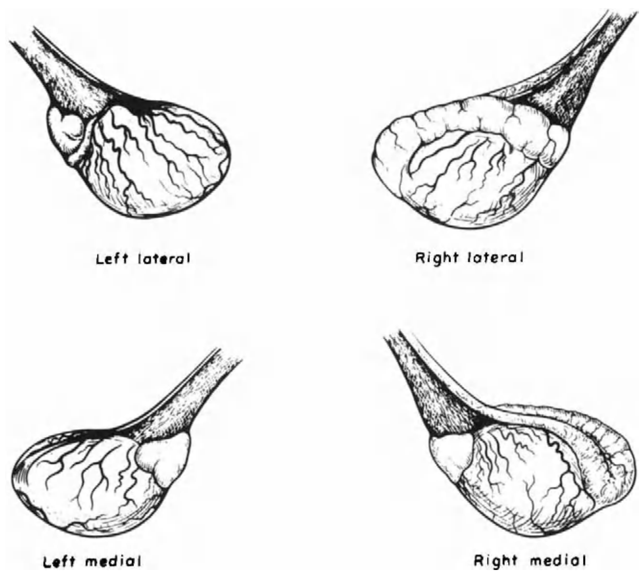

Fig. 16.8. Aplasia of the tail and body of the left epididymis of a dog. Acc. No. 6116.

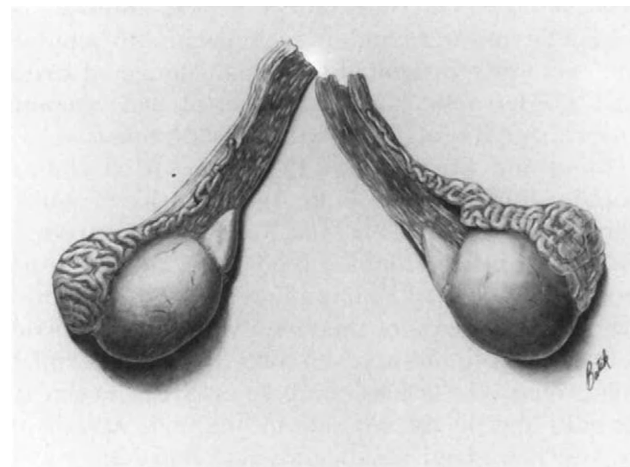

Fig. 16.9. Bilateral segmental aplasia of the canine deferent ducts. The epididymal tails are distended with sperm. Acc. No. 14495. (Provided by Dr. Ingemar Settergren.)

and serial section reconstruction of genital structures of 32 males considered to have cystic fibrosis, aged 3 days to 25 years, [and] gave the following results: absence of epididymal duct and vas deferens, atrophy and fibrosis of testis, 28; atresia of vas, atrophy of epididymis, 2; epididymal atrophy, status of vas uncertain, 1; and normal genital tract, 1."

Aplasia of the Deferent Duct

Boar. Heath *et al.* (1982) reported two cases of aplasia of the right deferent duct in swine. In both boars only the right testis and epididymis were in the scrotum. The material was collected in an abattoir and a search was not made for the possible presence of contralateral gonads in the abdominal cavity. The tail of the epididymis as well as a portion of the blindly ending deferent duct were distended with sperm in both animals.

Dog. I have seen single cases of unilateral aplasia of the ductus deferens in a Dachshund and a Golden Retriever and bilateral aplasia (Fig. 16.9) in a Schnauzer.

Bloom (1954) described and illustrated cystic distention of the canine ductus deferens. He stated that "Cystic dilatation of the vas deferens is usually unilateral and most frequently occurs at the entrance of the vas into the prostate. . . . As the cysts are observed occasionally in older dogs, the constriction possibly originates from previous inflammation." The malformation may be a congenital defect rather than an acquired lesion.

Man. In regard to aplasia of the deferent duct in man, Hanley (1962) reported that "When we reported our 9 cases of absent vasa in 1955 there were some 10 other cases in the world literature. However, our own series is now over 50 and we think this is a relatively common occurrence and one which should be possible to detect clinically before operation." All the anomalies reported by Hanley were bilateral. Apparently unilateral cases were not presented as fertility problems. Amelar *et al.* (1975) reported 101 cases of bilateral aplasia of the deferent duct in men. The sequential increase in the number of cases of aplasia of the deferent duct reported since 1955 suggests that the condition was generally overlooked previously.

Pigmentation

Bloom (1954) reported that "the cells lining the tubules of the epididymis of the dog often contain an iron-free, amorphous or granular, pinkish yellow or yellow pigment. . . . It occurs in normal as well as in atrophic cells of the epididymis."

Brown pigment granules accumulate in the cytoplasm of smooth muscle cells of the epididymis in aged bulls. They are usually overlooked on routine examination but can be demonstrated as a prominent lesion with the periodic acid–Schiff stain. They appear to be similar to lipofuscin (wear and tear) pigment that occurs in other organs of aged animals.

Adhesions

Donham and Simms (1931) examined the reproductive organs of 201 slaughtered bulls and found adhesions between the parietal and epididymal layers of the tunical vaginalis in 75.88% of the animals. The age of the bulls was not recorded but many were undoubtedly young because relatively few bulls were kept to an old age at that time. "No correlation could be established between the presence of these adhesions and the age, size, general condition, or breed of the bull being examined." The cause of the adhesions was not determined.

The adhesions appear first in the ventral part of the scrotum and tend to be more extensive in aged animals. Most of the adhesions are probably due to irritating substances that descend from the peritoneal cavity. Severe dense adhesions may occur as a result of trauma or periorchitis.

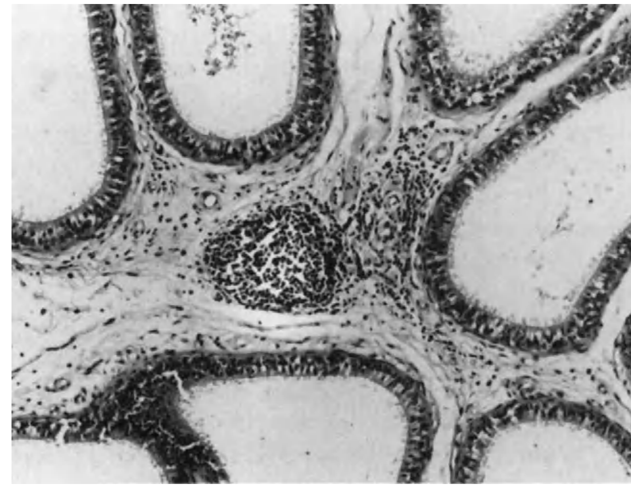

Fig. 16.10. Diffuse and focal accumulation of lymphocytes in the interstitial tissue of a bovine efferent ductule. ×81. Acc. No. 8730.

Torsion of the Appendix Epididymis

Torsion of the appendix epididymis has been reported in man but I am not aware of the occurrence of the condition in domestic mammals. Arcadi (1963) stated that the first case of torsion of this structure in man was reported in 1925 and "Since that time torsion of this embryonic remnant has been reported in only seven other patients." He reported a case in a 7-year-old boy who had pain and swelling in the scrotum. Exploratory surgery was conducted and a 0.5 by 1.0-cm, dark red, cystic mass was found attached to the right epididymis by a twisted pedicle. This may be an overlooked condition in domestic mammals.

Epididymitis

Lymphocytic Infiltrates

Diffuse and focal infiltrations of lymphocytes (Fig. 16.10) are present in the interstitial tissue of the efferent ductules of all mature domestic mammals. The lymphocytes appear to be a response to the phagocytosis of abnormal spermatozoa that can often be found in the tubular epithelium adjacent to interstitial lymphocytic foci (Fig. 16.11).

Dym and Romrell (1975) reported that in monkeys and rats lymphocytes "are found in the terminal portions of the seminiferous tubules near their junctions with the tubuli recti. Intraepithelial lymphocytes are also found in the tubuli recti, rete testis, ductuli efferentes, epididymis and ductus deferens. The ultrastructural morphology of these cells closely resembles that of the intraepithelial lymphocytes in the intestinal mucosa and those obtained from the lymph nodes, spleen, blood and thoracic duct." The majority of the cells appeared to be small, nonstimulated lymphocytes. It was suggested that "A resident population of immunocompetent intraepithelial lymphocytes may play some role in segregating sperm antigens from the general circulation. Our observation that the number of lymphocytes in the epididymal epithelium is very much less in 20- and 30-day-old sexually immature rats that do not yet have spermatozoa in the lumen is consistent with this speculation" (Dym and Romrell, 1975).

Wang and Holstein (1983) reported the presence of intraepithelial lymphocytes and macrophages in the efferent ductules and epididymis of men. They stated that these cells "may be an important compo-

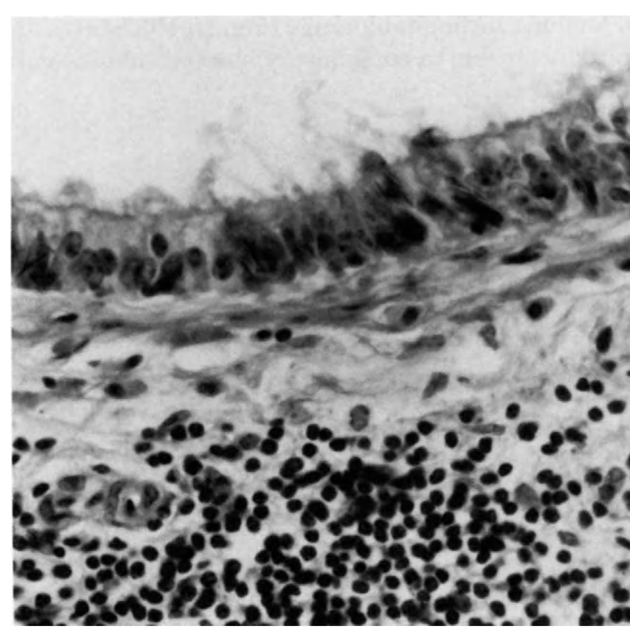

Fig. 16.11. Phagocytosis of spermatozoa by epithelium of the efferent ductule of a bull. Plasma cells and lymphocytes are in the interstitial tissue. ×418. Acc. No. 8730.

nent of the immunological barrier of the male reproductive duct. In the cauda epididymis, where spermatozoa degenerate, the intraepithelial lymphocytes are more numerous than elsewhere in the male reproductive tract. . . . [and] in old age when significant degeneration of spermatozoa occurs in the epididymis, the number of intraepithelial lymphocytes in the epididymis increases." This change is associated with the increase in degeneration of seminiferous tubules during old age.

Spermatic Granulomas

Spermatic granulomas develop secondary to sperm stasis in blind efferent ductules (Figs. 16.6, 16.12, and 16.13), accumulation of sperm in aberrant epididymal ducts (Figs. 16.14 and 16.15), sperm stasis secondary to adenomyosis of the epididymis, and secondary to infectious epididymitis. Sperm contain an acid-fast material that evokes a granulomatous response similar to that induced by the tubercle bacillus. The inflammatory reaction develops when sperm escape from the lumen of an efferent ductule or the epididymal duct into the adjacent connective tissue. Sperm granulomas have been mistaken for tuberculous lesions because of the presence of Langhans giant cells.

The predominant inflammatory lesions of the efferent ductules are spermatic granulomas and interstitial lymphocytic foci. Spermatic granulomas may be due to congenitally blind efferent ductules in which sperm accumulate and destroy the ductal epithelium or granulomas may develop following periductal inflammatory lesions that extend into the ductal lumen, causing its blockage (Fig. 16.16). Spermatic granulomas due to congenitally blocked tubules start to develop in sexually mature young animals, whereas acquired blockages may occur at any age after maturity.

Fig. 16.12. Sperm granuloma in the head of the right epididymis of a ram. The left epididymis is normal. Acc. No. 18042.

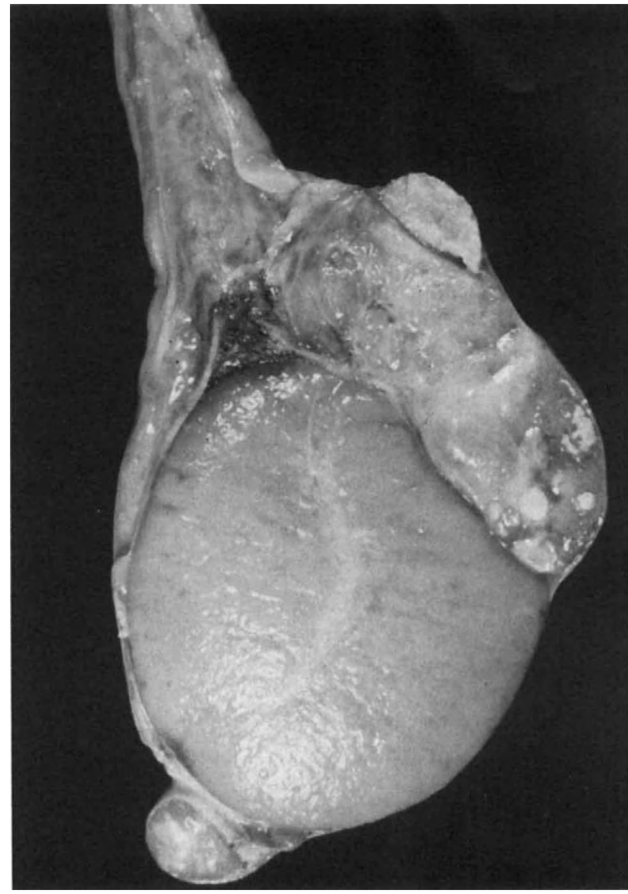

Fig. 16.13. Midsagittal section of ovine testis and epididymis with sperm granulomas in epididymal head. Acc. No. 18042.

Goat. Spermatic granulomas due to congenital malformation of the efferent ductules are a major cause of sterility in polled (hornless) goats. Ott (1937) reported that 20 to 25% of all male goats in breeding herds in Germany became sterile as a result of the development of sperm granulomas in the epididymis. Schönherr (1956) stated that one-third of a large number of sterile male goats had testicular hypoplasia and two-thirds had epididymal sperm granulomas. Ricordeau *et al.* (1972) reported that matings between polled goats produced at least 20% of males that were sterile because of obstruction of the efferent ductules.

The efferent ductules of a number of prepubertal polled goats should be dissected to determine the morphology of the ductules that result in ductal blockage. The study cannot be conducted on mature goats with advanced lesions because many of the

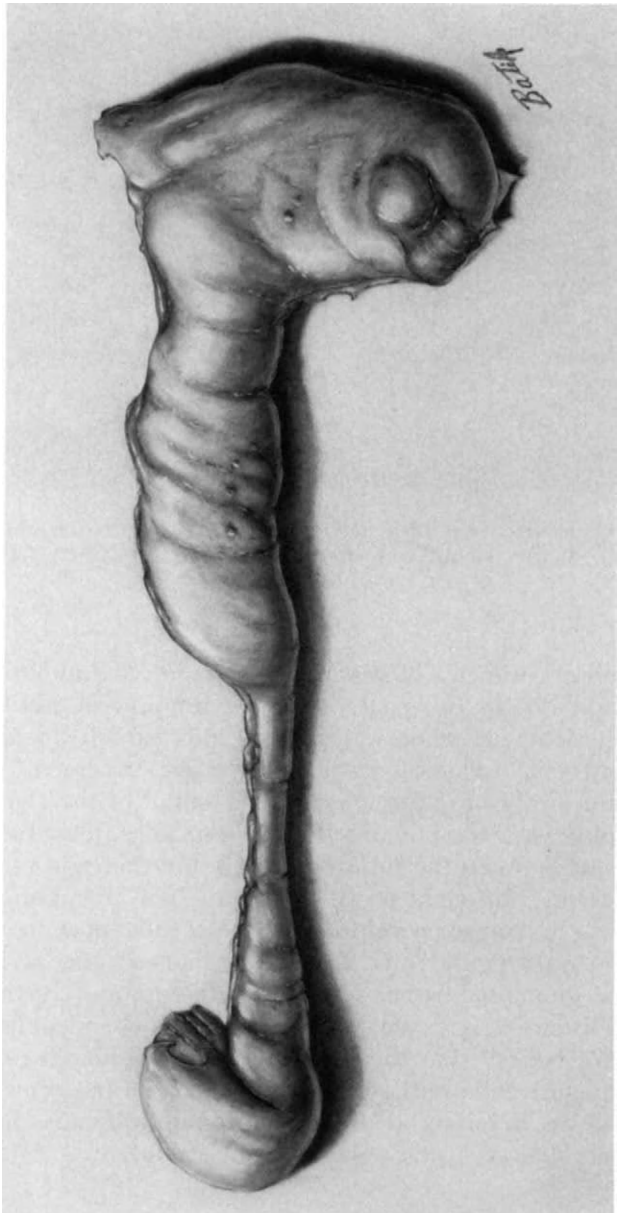

Fig. 16.14. Epididymal enlargement extending dorsally from the body of the epididymis in a bull. The enlargement is due to a sperm granuloma secondary to an aberrant ductule in the mid part of the epididymal body. Acc. No. 934.

ductules are destroyed by the diffuse inflammatory process.

Sperm granulomas may cause marked enlargement of the head of the epididymis. In some cases sperm penetrate the surface of the epididymis and produce granulomas on the tunica vaginalis. The content of sperm granulomas may be thin and watery or thick and puttylike. The lesion may be confused with an abscess based on gross examination. This is not the primary site of epididymal abscesses, however, and an impression smear will reveal that the

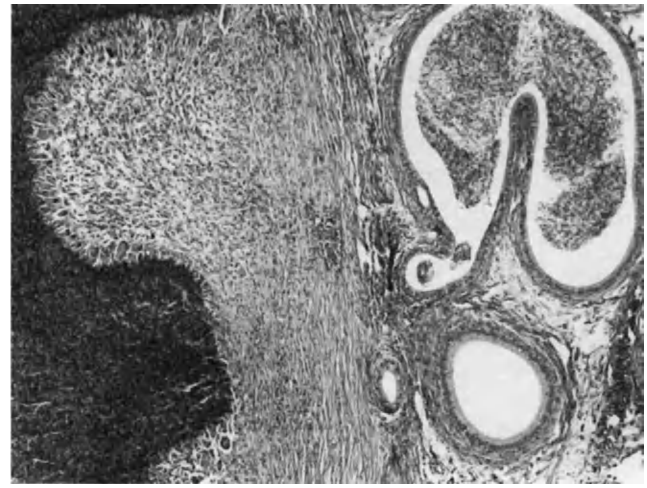

Fig. 16.15. Sperm granuloma that developed secondary to an aberrant duct in a goat. The duct extends from the epididymis to the granuloma. ×46. Acc. No. 19283.

content consists predominantly of spermatozoa and not inflammatory cells.

Bull. Blom and Christensen (1960) examined the reproductive organs of 2285 bulls and found spermiostasis in the ductuli efferentes of 2.1% of Danish Friesian bulls and 3.9% of Red Danish bulls. Wu (1981) reported a much higher incidence of lesions due to sperm stasis in the efferent ductules of bulls. He found that 206 (21.6%) of 953 bulls had sperm stasis, sperm granuloma, or scar formation. The incidence of these lesions increases with age.

The early lesion is stasis of sperm in one or more efferent ductules. The lumen of a blocked tubule

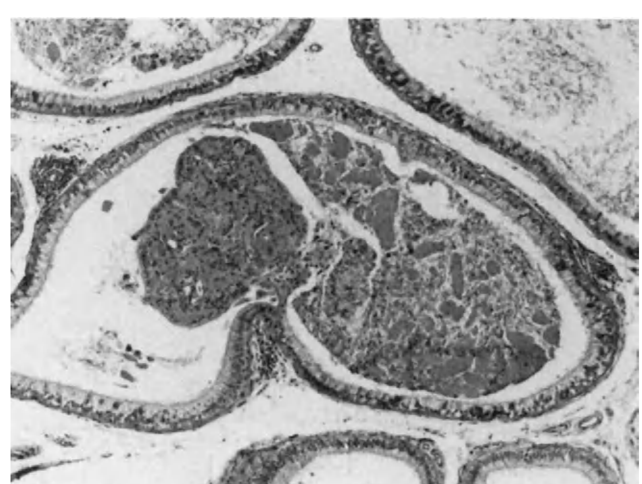

Fig. 16.16. Intratubular granuloma causing blockage of an efferent ductule in a bull. ×52. Acc. No. 10352.

may be distended with spermatozoa in some areas and filled with proteinaceous material in other areas. The affected tubules may become surrounded by collagenous connective tissue. When the integrity of the ductal wall is interrupted, sperm come in contact with connective tissue and a granuloma develops. Blockage that affects only one or a few ductules does not alter semen quality or quantity. Large granulomas completely block the passage of sperm to the epididymis.

During the process of healing of a small granuloma a stellate-shaped central cavity (Figs. 16.17 and 16.18), from which sperm have been phagocytized, will be present. The inflammatory cells diminish and an irregular-shaped area of fibrous tissue remains. These scars are usually overlooked on gross examination.

Stallion. Blue and McEntee (1985) reported the occurrence of epididymal sperm granulomas associated with adenomyosis and the migration of strongyle larvae in the stallion.

Urine-Induced Epididymitis

Man. Graves and Engel (1950) reviewed the clinical evidence indicating that the entry of urine into the epididymis of man results in the development of epididymitis. They stated that "This, we believe, occurs most commonly when an individual with a full or nearly full bladder is subjected to sudden and strenuous physical exertion with marked increase in intra-abdominal pressure. Likewise, it may occur in persons with prostatic or urethral obstruction who have been forced to employ the abdominal musculature to void."

Dog. Graves and Engel produced the condition in dogs. The animals were anesthetized, the ductus deferens surgically exposed, and one-fourth to one-half cubic centimeter of sterile urine was injected into the right ductus deferens. A similar amount of sterile physiological saline was injected into the left ductus deferens. Bilateral orchiectomy was performed 72 hours following the injections. The tail of the right epididymis was congested and there were fine adhesions between the tunica vaginalis and the right epididymis and right testis. Numerous polymorphonuclear leukocytes were present in the caudal portion of the right epididymis. There was marked edema of the interstitial tissue. The left epididymis and ductus deferens were normal. Graves and Engel concluded "We believe that the results obtained although not conclusive, do indicate that sterile urine forced down the vas deferens to the globus minor will cause inflammation of that portion of the epididymis."

Fig. 16.17. Sperm stasis in an efferent ductule in lower left and scar tissue in upper-central portion of the epididymal head in a bull. ×2.2. Acc. No. 15041.

Fig. 16.18. Scar with stellate central cavity in an efferent ductule from a bull with sperm stasis. ×22. Acc. No. 15041.

Epididymitis due to Infection

Infectious epididymitis is due to the same organisms that cause orchitis. The lesions usually begin in and occur more frequently in the epididymis than in the testis. For some unknown reason(s) the condition is frequently unilateral. The inflammatory lesions in infectious epididymitis usually start in the deferent duct and tail of the epididymis (Fig. 16.19). In longstanding cases the lesions may extend into its body and head. Sperm granulomas develop when the ductal epithelium is destroyed by the inflammatory process.

Epididymitis, at least in the bull and the boar, is usually secondary to seminal vesiculitis. This may also be true in rams and billy goats but the vesicular glands are not usually examined in these species. Epididymitis in the dog is often secondary to prostatitis.

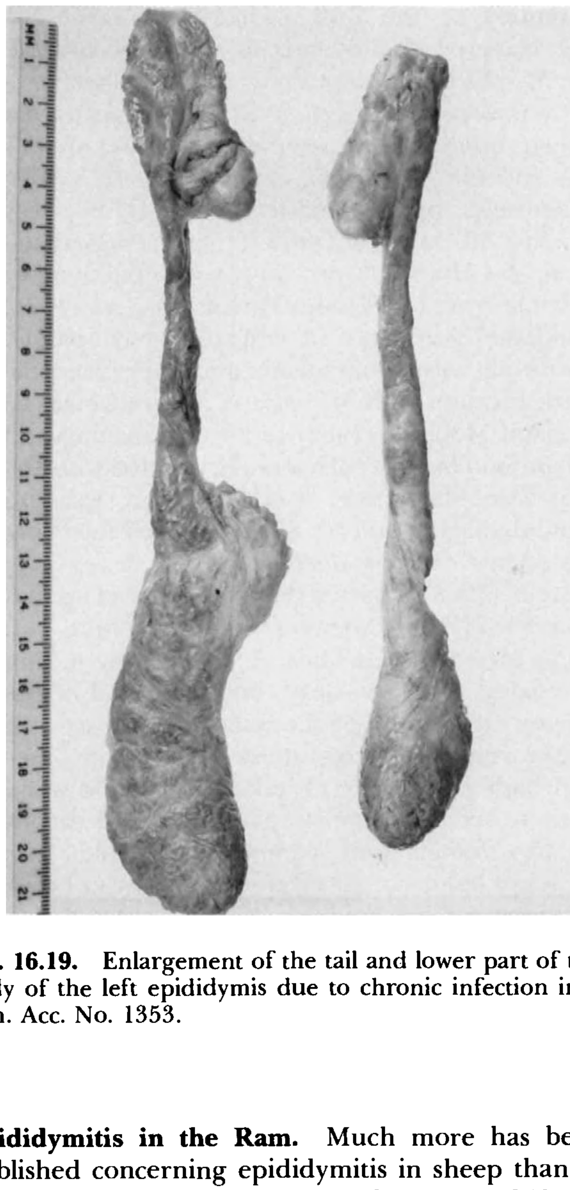

Fig. 16.19. Enlargement of the tail and lower part of the body of the left epididymis due to chronic infection in a ram. Acc. No. 1353.

Epididymitis in the Ram. Much more has been published concerning epididymitis in sheep than in other species of domestic mammals. Gunn (1942) recorded the incidence of epididymitis and spermatoceles found during the examination of more than 9000 rams in Australia. He stated that epididymal lesions were found in 5.3% of over 6000 rams in Queensland and in 5.7% of over 3000 rams in New South Wales. The lesions occurred most frequently in the tail of the epididymis and were usually unilateral.

Moule (1950) recorded the prevalence of epididymal lesions in sheep in northwestern Queensland; 17% of 972 rams had epididymitis.

Brucellosis in Sheep. Brucellosis in sheep is usually due to *Brucellas ovis*. Jebson *et al.* (1955) described the lesions of brucellosis in rams in New Zealand. They reported that the acute phase of the disease lasted for 2 to 4 weeks. During this time the scrotal content on the affected side was hot, swollen, and doughy. Postmortem examination revealed the presence of edema "in the loose scrotal fascia, fibrin-rich exudate in the cavity of the tunica vaginalis, together with serosal hyperaemia and early granulation tissue formation." The acute inflammatory reaction was less severe in some cases and consisted of a localized edematous swelling of the epididymis and the presence of fluid in the cavity of the tunica vaginalis. The chronic lesions consisted of enlargement of the tail of the epididymis and dense adhesions of the testicular tunics.

Kennedy *et al.* (1956) presented a more detailed description of the epididymal lesions in naturally occurring and experimentally induced cases of the disease. The most consistent abnormality involved the tail of the epididymis. "The enlargement of the epididymal tail varied in degree from barely perceptible to a four- to five-fold increase in size. The affected portion of the gland was firm, even hard, the normal globular contour became irregular, and palpable distinction from the distal pole of the testicle was diminished" (Kennedy *et al.*, 1956). The incised epididymal tail consisted of firm white tissue that in some cases contained single or multiple abscesslike spermatic granulomas containing creamy-tan to inspissated and caseous material. In some cases the entire epididymis was enlarged. Testicular atrophy was most severe when there were widespread adhesions of the tunics.

The earliest epididymal lesions "were necessarily obtained in this series from experimental animals which had been inoculated intratesticularly with cultures of the specific bacterium. They were strictly confined to the caudal epididymis, were essentially perivascular in distribution and consisted of perivascular edema and loose accumulations of lymphocytes" (Kennedy *et al.*, 1956). The changes in the epithelium consisted of edematous disorganization of the cells and infiltration of lymphocytes, plasma cells, and neutrophils. "Hydropic degeneration and lysis of epithelial cells in the edematous foci was followed by reorganization of the epithelium around them, with the formation of excessive intraepithelial cysts." Eosinophilic material and nuclear debris were present in some of the cysts. There was a marked increase in interstitial fibrous tissue in older lesions and spermatic granulomas were usually present. "Adhesions resulted in those cases in which sperm entered the cavity of the tunica vaginalis. . . . Primary inflammatory foci did not occur in the body or head of the epididymis or in the testicles. Atrophy of the testicles occurred in those cases of extensive adhesions; and, in these, there were foci of sperm stasis, intratubular granulomas, and calcification with surrounding fibrosis" (Kennedy *et al.*, 1956). Biberstein *et al.* (1964) reported that the lesions in the deferent duct were similar to those in the epididymis but sperm granulomas did not develop.

Pasteurella pseudotuberculosis. Jamieson and Soltys (1947) reported epididymo-orchitis due to *Pasteurella* *pseudotuberculosis (Yersinia pseudotuberculosis)* in rams. The disease occurred during July and August in Scotland. They stated that "In each case the disease was sudden in onset and was accompanied by a marked febrile reaction. In the initial stage, extreme tenderness around the scrotal area was evident, quickly followed by a developing unilateral enlargement. . . . In a number of instances the disease was fatal." They conducted postmortem examinations on three rams; two had died from the disease, and one was killed in the acute febrile stage. The testes were congested and covered by fine fibrinous deposits. The affected testes and epididymides weighed between 880 and 2115 g and the epididymides contained a gray purulent exudate.

Miscellaneous Bacterial Infections in Sheep. A variety of bacteria, in addition to *Brucella ovis*, have been isolated from the semen and epididymis of rams with inflammatory lesions in the genital organs. Reported isolates include: *Acinetobacter* spp., *Actinobacillus* spp., *Bacteroides, Actinomyces pyogenes (Corynebacterium pyogenes), C. pseudotuberculosis, Escherichia coli, Flavobacterium, Haemophilus* spp., *Haemophilus agni, Histophilus ovis, Micrococcus luteus, M. varians, Moraxella* spp., *Pasteurella haemolytica, P. multocida, P. pseudotuberculosis, Staphylococcus* spp., *Streptococcus* spp., various *Enterobacteriae* and *Pseudomonas* spp., *Brucella abortus*, and *B. abortus* (strain 19) (Ekdahl *et al.*, 1968; Jansen, 1980a; Lozano, 1986; Walker *et al.*, 1986).

Most of the reports dealing with infection of the reproductive organs of sheep do not mention the internal genital organs. Thus one is led to believe that infection of the reproductive tract of the ram occurs primarily in the epididymis. Jansen (1980b) demonstrated that infection of the reproductive organs, as in the bull and boar, occurs more frequently in the vesicular glands than in the epididymides. Necropsies were conducted on 100 rams that were culled because of "palpable lesions of the external genitalia, the presence of neutrophils and bacteria in their semen, and/or poor breeding performance." Only rams from flocks that were free of *Brucella ovis* were selected. Of the 100 rams, 63 had ampullitis, 60 had vesiculitis, and 42 had epididymitis. Jansen (1980b) stated that "While it is true that in some rams only one or both epididymides were affected clinically, in others these organs were completely normal and free of bacteria, but their ampullae and vesicules seminales showed marked histopathological changes. . . . It was impossible to associate a particular histopathological lesion with a single bacterial species, because in many instances the same type of lesion was caused by different bacteria. Also, more than one type of organism was often isolated from an affected organ." Almost any pathogenic organism can, and on occasion does, cause epididymitis in rams.

Epididymitis in the Bull. The major causes of chronic bacterial epididymitis in cattle are *Brucella abortus, Mycobacterium tuberculosis*, and *Actinomyces pyogenes (Corynebacterium pyogenes)*. Other organisms that have been reported to cause epididymitis and orchitis in bulls include *Streptococci, Staphylococci, Escherichia coli, Hemophilus* spp., and *Salmonella* spp. (Humphrey and Ladds, 1975a). Storz *et al.* (1968) reported the isolation of *Chlamydia* from bulls with epididymitis. Al-Aubaida *et al.* (1972) and Parsonson *et al.* (1974) reported the occurrence of vesiculitis and epididymitis in bulls with spontaneous and experimentally induced infection with *Mycoplasma bovigenitalium*. La Faunce and McEntee (1982) reported vesiculitis and epididymitis in bulls experimentally infected with *Mycoplasma bovis*. Mészáros *et al.* (1976) found vesiculitis and epididymitis in bulls that had ingested feed contaminated by *Candida guilliermondii*.

Ball *et al.* (1968) reported the occurrence of epididymitis in 55 (71%) of 78 young bulls from a herd with a high incidence of vesiculitis. A single tissue section was prepared from the head, body, and tail of the epididymis from some of the bulls and two sections were prepared from each of these regions from other bulls. A higher incidence of lesions was found when more tissue sections were prepared. Most of the inflammatory lesions were comparatively mild. The frequency of lesions in the efferent ductules and various segments of the epididymis was not stated and the etiology of the lesions was not determined. It is quite possible that the highest incidence of lesions occurred in the connective tissue of the efferent ductules and may have been due to phagocytosis of sperm.

Anderson *et al.* (1951) described the gross and microscopic lesions of three Friesian bulls with "a specific venereal infection ('epivag')." The bulls were known to have had epididymitis for at least 6 months when they were slaughtered. The testes were atrophic and chronic inflammatory lesions were present in the vesicular glands, prostate glands, ampullae, and epididymides. In regard to the epididymal lesions, they stated that "In all cases the changes were of such extent and of such long standing that it was impossible to speculate on the form of the primary lesion. . . . The tubules were dilated but contained few or no spermatozoa. Where present the content of the tubules consisted almost exclusively of a few eosinophils with some structureless cell debris and rarely a few recognisable spermatozoa." The epithelium was frequently invaded by eosinophils and lymphocytes. The connective tissue was diffusely infiltrated by large mononuclear cells, plasma cells, and lymphocytes. There was a marked increase in the interstitial fibrous tissue. The cause of the condition has not been established. Theodoridis (1978) suggested "that 'epivag' may be due to infection with more than one infectious agent, including viruses and other micro-organisms." In regard to the name of the disease, Hudson (1952) stated that "Some years ago the writer coined the term 'epivag' for epididymitis and vaginitis as a temporary name for use in the Kabete laboratory. The word is ugly and liable to be converted into the ridiculous 'epivaginitis'; but it must be mentioned, since it has now crept into official reports." The cause(s) of the disease is not known.

Epididymitis in the Stallion. Little has been published concerning epididymitis in the stallion. Schebitz and Hansen (1949) reported unilateral epididymitis caused by *Salmonella abortus equi* in the donkey. They concluded that a traumatic lesion is the prerequisite for a hematogenous infection of the epididymis. van der Schaaf and Hendrikse (1963) reported infection of the tail of the epididymis by *Streptococcus zooepidemicus* in the stallion.

Epididymitis in the Dog. Epididymitis in the dog may occur with infection by various bacteria, including *Brucella canis, B. abortus, B. suis, Escherichia coli, Proteus vulgaris, Streptococcus* spp., and *Staphylococcus* spp. The epididymis is usually enlarged uniformly throughout its length (Fig. 16.20) by the time the condition is diagnosed. Sperm granulomas and abscesses may be present. If they are not evident on gross examination the chronic inflammatory lesion is often mistaken for a neoplasm by inexperienced veterinarians. Neoplasms of the epididymis are extremely rare.

Epididymitis is often associated with distemper. Intranuclear and cytoplasmic inclusions are present in the tubular epithelium.

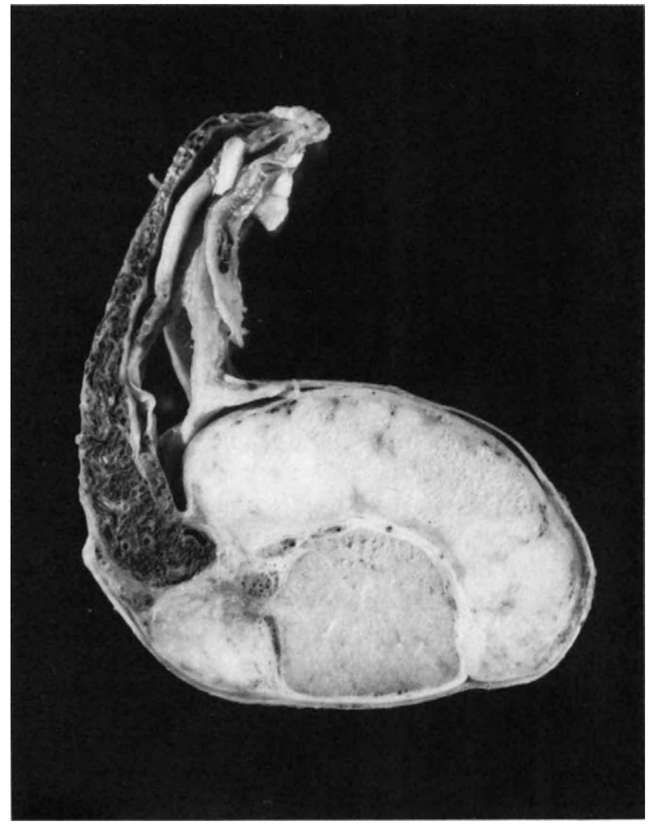

Fig. 16.20. Midlongitudinal section of spermatic cord, epididymis, and testis of a dog. Marked enlargement of the entire epididymis is due to chronic epididymitis. Acc. No. 17201.

Progressive and Regressive Processes

Atrophy

Bloom (1954) reported atrophy of the epididymal epithelium in dogs with testicular atrophy. "Coexistent with the tubular changes, the interstitial connective tissue is often increased and may be hyalinized." Senile atrophy of the testes "is especially common in dogs over 10 years of age and is occasionally seen in cats over 12 years of age."

Squamous Metaplasia

McEntee and Olafson (1953) reported keratinizing squamous metaplasia of the epididymis in bulls with hyperkeratosis (highly chlorinated naphthalene poisoning). They stated that "The pseudostratified columnar epithelium of the epididymis gradually stratifies, and in some areas the lumen becomes plugged with keratin. . . . The epididymis becomes so markedly enlarged and hardened that the condition may be diagnosed by palpation in the living animal." The efferent ductules do not undergo metaplasia. The lesion commences in the head of the epididymis and gradually progresses to the epididymal tail. Metaplasia does not occur in the epididymis of the poisoned ram.

Osseous and Cartilagenous Metaplasia

Bone formation occurs along the edge of the head and body of the epididymis in some old bulls. This appears to be a lesion induced by prolonged rubbing between the tunics. I have seen cartilagenous metaplasia in the equine epididymis.

Epithelial Hyperplasia (Intraepithelial Lumina, Intraepithelial Cysts)

Intraepithelial lumina are present in the epididymal epithelium of sexually immature animals as a stage in development and in sexually mature animals as a hyperplastic lesion. Scott *et al.* (1960) described and illustrated intraepithelial vesicles in the epididymis of cats that were fed unsupplemented raw heart. The cats had underdeveloped testes similar to those of sexually immature animals.

Mawdesley-Thomas and Urwin (1967) reported three cases of epithelial hyperplasia of the epididymis in a series of 4000 sexually mature dogs. The affected dogs were healthy and the lesions were not associated with an experimental procedure. They stated that the dogs were sexually mature but the ages were not stated.

James and Heywood (1979) examined the epididymides of 198 dogs that were between the ages of 37 weeks and 7.75 years. They stated that "Hyperplasia of the ductal epithelium in the epididymis was not apparent among dogs aged less than 125 weeks. This change was recorded in approximately 75% of dogs attaining a mean age of 7.75 years."

Epithelial hyperplasia occurs in the epididymis of all species of domestic mammals and the incidence of the lesion tends to increase with age. I believe that the lesion is a precursor of epididymal adenomyosis.

Adenomyosis

Adenomyosis of the epididymis is the invasion of the muscle of the epididymal duct by the lining epithelium (Fig. 16.21). The lesion is usually overlooked by pathologists because the epididymis is seldom examined histologically unless there are gross lesions. This oversight applies to man as well as domestic mammals. Mitchinson *et al.* (1975) remarked that in man "The epididymis is a neglected organ at necropsy." Adenomyosis of the epididymis is caused by excessive exposure to estrogen under either natural or experimental conditions.

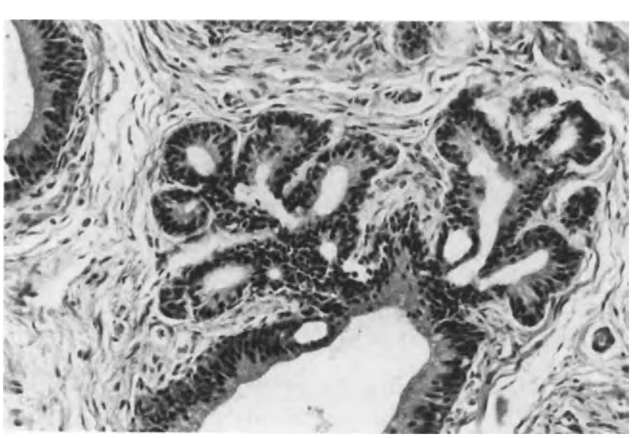

Fig. 16.21. Adenomyosis of the canine epididymis. Numerous branching tubules extend from the epididymal lumen. ×178. Acc. No. 14634.

Rabbit. Bern (1949) reported and illustrated glandular proliferation of the epithelium of the ductus deferens and epithelial invasion of the ductal muscle and connective tissue in rabbits on long-term estrogen treatment. The lesion also occurred in the epididymis. He stated that "The cancerous nature of these changes is open to question, since their independence of continued estrogenization was not determined." My experience with the occurrence of the lesion in domestic mammals indicates that it is not a precancerous lesion.

Mouse. Dunn and Green (1963) reported lesions of the epididymis in mice that were given injections of diethylstilbestrol on the day of birth and necropsied at 13 to 26 months of age. Epididymal lesions were found in more than half of the male mice. The earliest lesion was vacuolation of the epithelial cells. In 13- to 26-month-old mice "Single or multiple cysts, often bilateral, were the commonest finding." Although they did not allude to it in the text, adenomyosis of the epididymis is evident in their Figs. 6 and 8.

Tucker and Baker (1967) published a photograph of advanced adenomyosis of the epididymis in an old mouse and referred to the condition as diverticulosis.

Dog and Bull. Under the heading of tumors of the epididymis in the dog, Bloom (1954) mentioned "adenomatous proliferation of minute, multiple, alveolar structures, with or without lumens, in the immediate vicinity of coils of the ductus epididymis. These apparently originated from the ductus and are lined by similar epithelium."

McEntee (1974) reported the occurrence of adenomyosis of the epididymis in the dog and the bull. The lesion was found in 43 (6.2%) of 695 bulls from one artificial insemination center and in 13 (48.2%) of 27 dogs with sustentacular (Sertoli) cell tumors. Lennart Krook and I have produced the condition experimentally in dogs and bulls by the long-term administration of estrogens. Advanced adenomyosis of the epididymis results in the formation of sperm granulomas in bulls (Fig. 16.22) but not in dogs with sustentacular cell tumors because dogs are more sensitive to estrogens than bulls. Bulls can be treated with diethylstilbestrol for years and continue to produce some sperm. On the other hand, estrogen causes advanced testicular degeneration in the dog and a complete inhibition of sperm production; thus the epididymis is devoid of sperm (Fig. 16.23). Adenomyosis of the epididymis also occurs in some dogs without sustentacular cell tumors and they may develop sperm granulomas (Fig. 16.24).

Nascimento *et al.* (1979b) found adenomyosis of the epididymis in 6 (3.8%) of 158 mongrel dogs in Brazil. A sperm granuloma was present in the epididymis of one of the dogs.

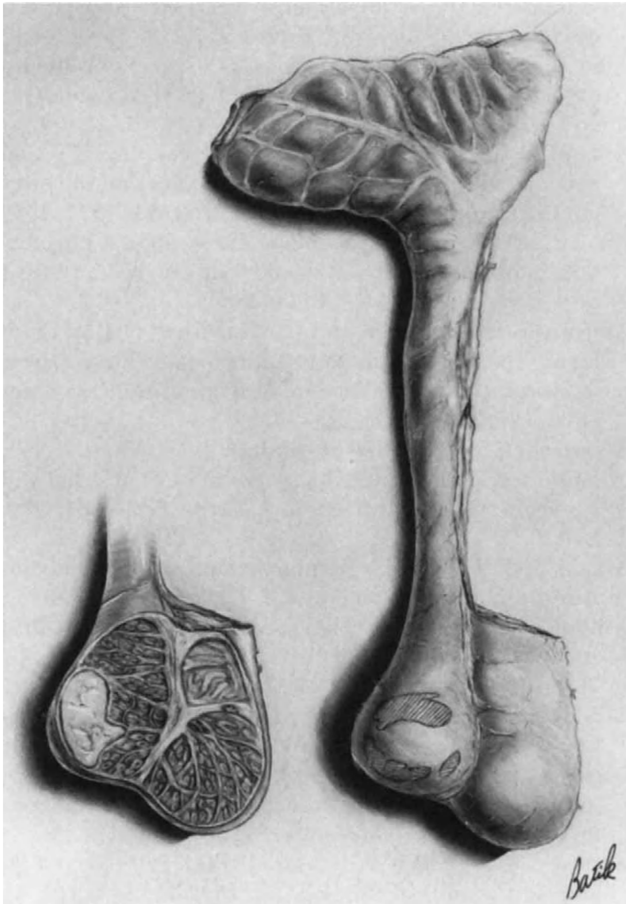

Fig. 16.22. Sperm granuloma secondary to adenomyosis of the epididymal tail of a bull. Acc. No. 13628.

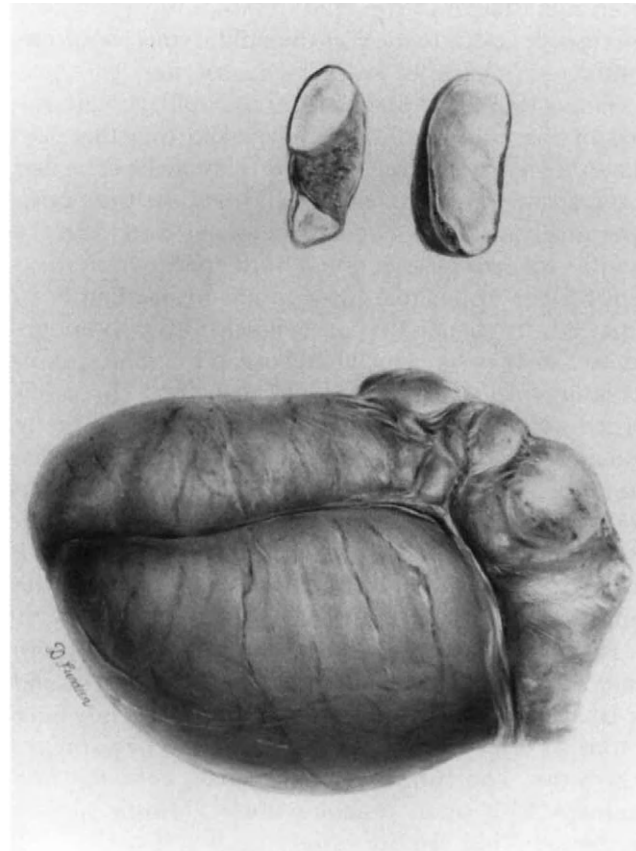

Fig. 16.24. Sperm granulomas due to adenomyosis of the canine epididymis. Acc. No. 932.

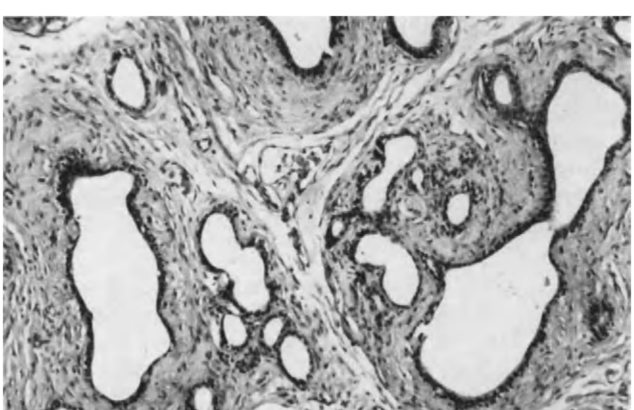

Fig. 16.23. Adenomyosis of the epididymis of a dog with advanced testicular degeneration and an absence of sperm. Numerous small ducts extend from the epididymal lumen through the smooth muscle and into the adjacent connective tissue. ×89. Acc. No. 14137.

Connell and Donjacour (1985) reported the effects of administering 400 μg of estradiol benzoate to Beagle dogs every fourth day from 5 to 20 weeks of age. The estrogen-treated dogs had significantly larger epididymides and significantly smaller testes at 20 weeks of age. In regard to the estrogen-treated dogs they stated that "The tubules of the caput epididymidis are irregular in shape and sometimes have outpocketings or divertuli." Their illustration of this lesion is that of early adenomyosis. The increased weight of the epididymis in treated dogs was due to a proliferation of interstitial fibrous tissue.

Other Species of Domestic Mammals. I have seen adenomyosis of the epididymis in the ram, goat, and stallion. It appears to occur at an earlier age in the horse than in other animals. The condition probably occurs in all species of domestic mammals.

Neoplasms

Primary neoplasms of the epididymis are rare in domestic mammals. Malignant neoplasms of the testis often metastasize to the epididymis. Thus gross and microscopic examination of the epididymis should be conducted in cases of testicular neoplasia.

Salm (1969) reported bilateral papillary carcinomas of the epididymis in a 7-year-old dog that had bilateral scrotal swellings for several months. The dog was castrated and remained well for some time postoperatively. It later developed ascites and died 14 months following castration. "Both epididymides, except for the upper margins of their heads, had been replaced by firm, fleshy, yellowish-grey homogeneous tumor tissue which had spread long the spermatic ducts up to the excisional margins. Three enlarged neoplastic lymph-glands were attached to one gonad. Low papillary projections were noted on each tunica-vaginalis" (Salm, 1969). Postmortem examination revealed metastatic tumor nodules in the liver, on the parietal peritoneum, on the mesentery, in the paraaortic and mesenteric lymph nodes, and in the lung.

In regard to the primary neoplasm Salm (1969) stated that "in some areas the growth is either solid or composed of small acini or tubules, but elsewhere it consists of cystic glands with large solid or papillary ingrowths. The tumor cells are small, cuboidal and uniform, with small vesicular nuclei. Mitotic figures are present, but are not numerous."

I have examined one carcinoma of the epididymis of a dog and one from a bull. I have seen three mesotheliomas that were located on the epididymis and testis of bulls. Two had primary lesions in the peritoneal cavity and one was confined to the testis and epididymis. My collection of epididymal tumors also includes a lipoma from a horse.

Bloom (1954) mentioned that malignant lymphomas may invade the epididymis. He also reported two cases of epididymal fibromas from the dog.

Metastases to the epididymis have occurred from primary neoplasms of the prostate, kidney, stomach, and colon in man (Wachtel and Mehan, 1970).

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Chapter 17

Bulbourethral, Vesicular, and Prostate Glands

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Anatomic Features

Bulbourethral (Cowper's) Gland

The bulbourethral glands of man were described by Mr. William Cowper, F.R.S., in the "Philosophical Transactions" of the British Royal Society, Number 258, page 364, November 1699 (see Cowper, 1700). The original article was reproduced by Church (1938). The bulbourethral glands are paired structures that lie dorsally on either side of the pelvic urethra near the ischiatic arch. They are present in all domestic mammals except the dog. The glands are seldom examined by pathologists.

Ruminants. According to Schummer *et al.* (1979), the bulbourethral glands of the "bull are about 2.8 cm. long craniocaudally and 1.8 cm. thick dorsoventrally. They lie on the dorsal surface of the urethra opposite the ischiatic arch and are covered by the proximal part of the thick bulbospongiosus muscle [Fig. 17.1] so that under normal circumstances the gland cannot be felt rectally. Each lobe has an excretory duct that opens on the dorsal wall of the urethra under cover of a caudoventrally-directed fold of mucous membrane." The bulbourethral glands of the ram and buck are about 1 cm in diameter. The mucous secretion of the glands is discharged prior to ejaculation in ruminants and lubricates the vagina.

It is a tubuloalveolar gland in the bull and ram and a compound tubular gland in the goat. Dellman and Brown (1976) stated that "in the bull and the ram short connecting pieces link the secretory portions to the collecting ducts, which are lined by a simple cuboidal epithelium (sometimes also secretory). In the goat these secretory portions empty directly into these ducts. Smooth muscle cells are particularly abundant within the interstitium."

Boar. The bulbourethral glands in the boar consist of two cylindrical lobes that are about 17–18 cm long and approximately 5 cm in diameter (Schummer *et al.*, 1979). They lie on either side of the pelvic urethra and are covered by a thin layer of bulboglandularis muscle. The glandular tissue consists of compound tubuloalveolar epithelium and the tubules and ducts are lined by columnar epithelium. The glands contain collecting spaces filled with a clear mucoid secretion. Each gland has an excretory duct that leaves the caudal part of the gland and opens into the urethra.

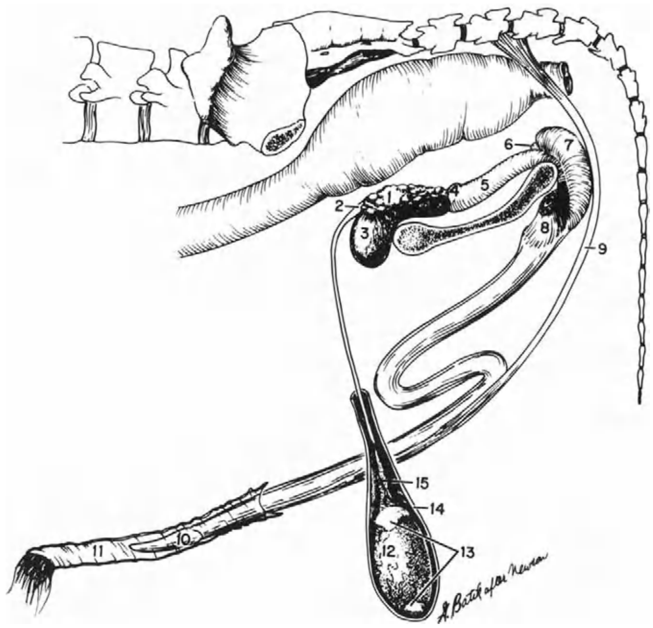

Fig. 17.1. Reproductive organs of the bull; 1, vesicular gland; 2, ampulla; 3, urinary bladder; 4, prostrate; 5, urethral muscle surrounding the pelvic urethra; 6, bulbourethral gland; 7, bulbospongiosus muscle; 8, ischiocavernosus muscle; 9, retractor penis muscle; 10; glans penis; 11, preputial membrane and cavity; 12, testis; 13, epididymis; 14, scrotum; 15, spermatic cord. Acc. No. 14048. (From Hansel and McEntee, 1977.)

Stallion. The bulbourethral glands of the stallion are club-shaped and are attached to the dorsolateral surface of the urethra near the pelvic outlet. They are approximately 4 to 5 cm long and 2 to 3 cm wide. The gland is compound tubuloalveolar and produces a serous secretion with traces of mucus. Each gland has several excretory ducts.

Cat. The glands in the cat are about 5 mm in diameter and lie dorsolaterally on the urethra at the level of the ischiatic arch. They are covered by the striated compressor muscle and have a very thin fibrous capsule. It is a compound tubular gland, the secretion is mainly mucous with some serous fluid, and it contains interlobular fat cells and cavernous spaces.

Vesicular Gland (Seminal Vesicle)

The term seminal vesicle is used frequently and incorrectly to denote the vesicular gland. The latter term should be used instead of seminal vesicle because the vesicular gland does not serve, as was thought originally, as a normal storage place for semen. The vesicular glands are true vesicles in horses, and compact lobulated glands in cattle, swine, sheep, and goats, and are absent in dogs and cats.

Ruminants. The vesicular glands are the largest accessory genital glands in the bull, ram, and buck goat. According to Schummer *et al.* (1979), the gland "is hard and compact, has an uneven surface, and in the bull an irregular elongated form, often bent on itself or S-shaped. The vesicular gland of small ruminants is shorter and more rounded. In the bull, the gland is 10–12 cm long and 1.5–3.5 cm thick, having a total weight of 45–80 gm. In small ruminants, the vesicular gland is 2.5–4 cm long, 2–2.5 cm wide, and 1–1.5 cm thick."

The vesicular gland of the bull is a compact lobulated organ. Dellman and Brown (1976) stated that "Intralobular secretory ducts drain the slightly coiled tubular portions of the tubuloalveolar gland, and in turn are drained by the main secretory duct. The secretory columnar cells have small lipid droplets and glycogen and give a positive alkaline phosphatase reaction. . . . The basal cells are characterized by large lipid droplets, often in an infranuclear position." The lipid droplets are not present in castrated nor in young bulls and do not become numerous until the bull is 4 to 5 years of age.

Dellman and Brown reported that "Lipid droplets in the basal cells are absent in the ram, but may be present in the buck. During the breeding season the epithelium of the vesicular gland of the buck is considerably higher than during the nonbreeding season."

Boar. According to Schummer *et al.* (1979), the vesicular gland of the boar "consists of two pyramidal masses that are attached to each other medially by connective tissue. Each of these masses is 12–17 cm long, 6–8 cm wide, and 3–5 cm thick, and is oriented so that its base is cranial and its apex caudal. . . . On cut surface are seen large collecting spaces which can store considerable amounts of secretion. The collecting ducts of each side of the gland unite to form an excretory duct, which opens on the colliculus seminalis close to the ipsilateral ductus deferens." The secretory epithelium in the boar is folded and the tubular lumina are wide.

Stallion. The vesicular glands of the stallion are 10 to 15 cm long and 3 to 6 cm in diameter. They have a large central cavity into which the mucosa forms folds and crypts. The glands decrease in diameter as they converge caudally.

Prostate Gland

The prostate gland is present in all species of domestic mammals. It is most important in the dog as far as diseases are concerned. The prostate of most domestic mammals consists of two parts, a body situated behind the entrances of the ductuli deferentia and the vesicular glands into the urethra and a disseminated portion (pars disseminata) consisting of glandular elements extending along the urethra and lying beneath the urethral muscle.

According to Dellman and Brown (1976), "The secretory tubules, alveoli and intraglandular ducts of the prostate gland are lined by a simple cuboidal or columnar epithelium with occasional basal cells. The simple epithelium changes from stratified columnar to transitional toward the terminal portions of the ducts. . . . The tall columnar cells frequently possess bleb-like apical protrusions."

Ruminants. The bovine prostate gland is bilobed and is located on the dorsal surface of the urethra caudal to the vesicular glands. The body portion of the gland protrudes slightly above the urethralis muscle. The disseminate portion is enclosed by the urethralis muscle and surrounds approximately 12 cm of the urethra.

The ram and the buck goat have only a disseminate gland. In the ram it only covers the dorsal and lateral walls of the urethra.

Boar. The body of the porcine prostate gland is a relatively small, flat mass located on the dorsal surface of the urethra. The major portion of the gland is in the disseminate portion, which is covered by the urethralis muscle.

Stallion. Schummer *et al.* (1979) stated that the prostate gland of the stallion is "retroperitoneal and consists of two firm, nodular lobes connected across the midline by an isthmus that is about 3 cm long. Each lobe is 5–9 cm long, 3–6 cm wide, and about 1 cm thick. A disseminate part is absent. Numerous ductules carry the prostatic secretion to small slitlike openings on the side of the colliculus seminalis."

Dog. Gordon (1961) investigated the topographic anatomy of the prostate gland of 140 dogs (newborn to 19 years old) and eight 52-day old fetuses. She stated that "In animals which were prenatal, newborn, and less than 2 months old, the gland was abdominal in position; whereas, in pups 2 to 8 months old, the gland was pelvic in position. After sexual maturity, the prostate increased in size and, with increasing age, changed its position from pelvic to abdominal. After the age of about 10 years, the prostate can be considered as an abdominal organ."

The canine prostate gland is compact and is relatively large compared to the glands of other species of domestic mammals. Berg (1958a) stated that the prostate gland of the dog "is almost globular in form, symmetrical, yellowish in colour, of a firm or tense-elastic consistency and with a distinct median furrow (sulcus dorsalis) dorsally, which may be easily palpated per rectum, indicating a right and left lobe."

According to Schummer *et al.* (1979), "The disseminate part is represented by a small number of prostate lobules in the wall of the urethra. The numerous excretory ducts of the prostate open lateral to the colliculus seminalis."

Cat. Bloom (1954) stated that the prostate of the cat "is somewhat bulb-shaped and is about 10 to 12 mm in length. Although the prostate of the cat is described as bilobed, it appears to consist of four somewhat flattened spherical lobes. The cranial lobes are separated from the caudal ones by a relatively wide connective tissue septum. A longitudinal median groove divides the lateral lobes." The gland covers the urethra dorsally and laterally. The disseminate part consists of small lobules that extend into the urethral muscle (Aitken and Aughey, 1964).

Congenital Anomalies

Bulbourethral Gland

Bagshaw and Ladds (1974) reviewed the literature on pathology of the bulbourethral glands of the bull and examined the reproductive organs of 521 slaughtered bulls from Queensland and the Northern Territory of Australia. They found four cases of unilateral aplasia and four cases of hypoplasia of the glands. Fusion of the bulbourethral glands was found in nine bulls. They stated that the fusion "mostly involved only the posterior parts of the glands. A central collecting duct for each gland was present, and on all occasions there were 2 excretory ducts." Melanosis of the bulbourethral gland was found in one bull.

Vesicular Gland

Segmental aplasia is the main congenital anomaly affecting the vesicular glands of domestic mammals. This malformation in the bull has been reported by Gilman and Hopper (1925), Blom and Christensen (1947, 1951, 1956), Ashdown (1958), McEntee (1958), van der Sluis (1961), Kanagawa *et al.* (1961), Haase (1962), Carroll *et al.* (1963), Bane (1968), Galloway and McFadden (1969), and Arthur (1975). Although the left vesicle or both may be affected, right-sided aplasia is more common and it appears to be a hereditary defect. The condition is frequently accompanied by aplasia of the epididymis on the same side. (See Chapter 16 for details of concomitant lesion.)

Hypoplasia of the vesicular gland may occur in association with normal ampullae (Fig. 17.2) and epididymides.

Blom (1979b) found malformations or rare anatomical deviations of the accessory reproductive organs in 10 of 24 bulls with vesiculitis. The major malformations of the vesicular glands included segmental aplasia, segmental hypoplasia, and accessory glands. The other defects were asymmetrical implantation of the ampullae and persistent uterus masculinus in open contact with the urethra on or near the colliculus seminalis. A common feature of all the cases was that the defects involved the orifices of the colliculus seminalis. Blom stated that "these abnormalities may disturb the normal closing function of the colliculus seminalis, and thus perhaps represent a *locus minoris resistentiae* to possible infectious agents." He also reported that "Genetic factors should be considered in relation to the pathogenesis of vesiculitis. Of the total of 32 bulls examined, 22 were of the Friesian breed. Of these 22, four were sons of and six others closely related to, a certain outstanding and therefore widely used bull."

I have seen unilateral double vesicular glands (Fig. 17.3) in three Holstein-Friesian bulls and one Hereford bull. The right gland was affected in one Holstein bull and the left gland was double in the other animals. Jones *et al.* (1964) reported the presence of five accessory lobes of the right vesicular gland of a Friesian bull.

Prostate Gland

Bagshaw and Ladds (1974) found an anomaly of the prostate gland in 1 of 521 bulls. They stated that "a peduncle approximately 1 cm long and 0.5 cm in diameter projected into the lumen of the pelvic urethra in the region of the seminal colliculus. This peduncle resembled prostate gland histologically."

Cysts

Bulbourethral Gland

Blom and Christensen (1958) reported the occurrence of bilateral cysts in the bulbourethral glands of two Danish Friesian calves and a 4-year-old Jersey

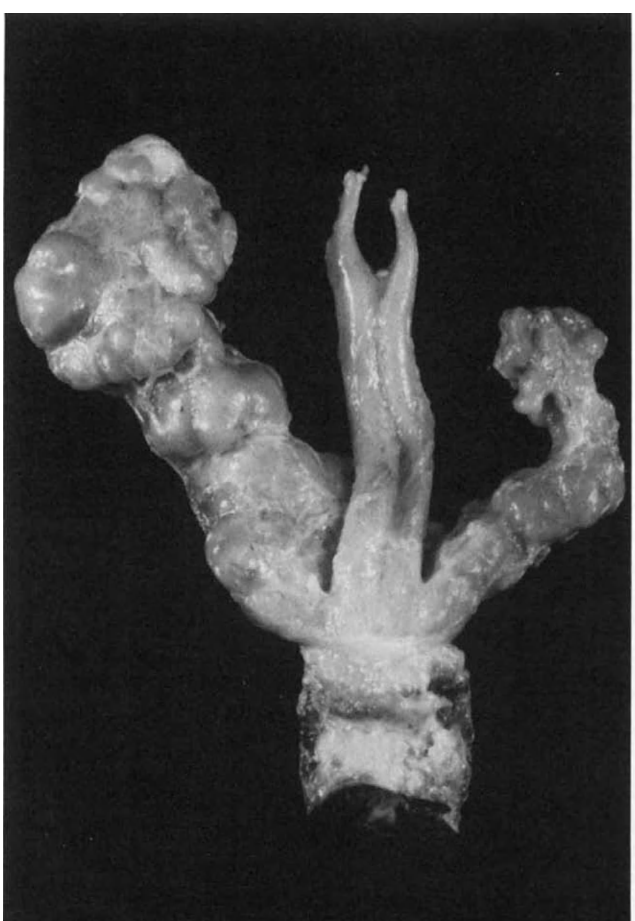

Fig. 17.2. Hypoplasia of the right vesicular gland of a bull. Acc. No. 19242.

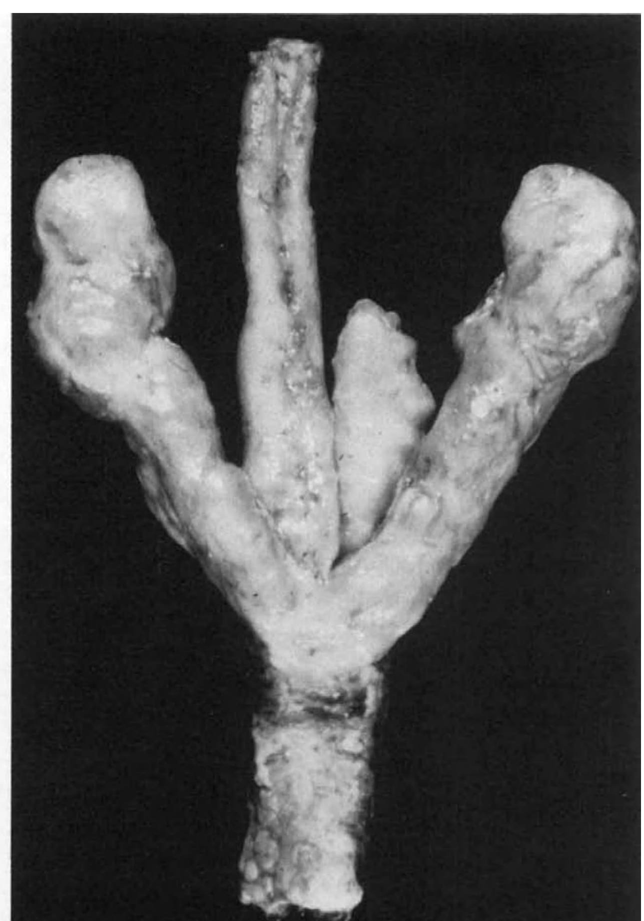

Fig. 17.3. Vesicular glands of a bull with bilateral vesiculitis and duplication of the right gland. Acc. No. 11883.

bull. They stated that the cysts in the calves were the size of large peas. The glands of the Jersey bull were enlarged. "The gland on the right side measured 22 × 18 mm and on left 28 × 19 mm (length and breadth). In the gland on the right side were 2–3 cystic distentions 7–8 mm in diameter; on the left side were somewhat similar conditions, as well as a single rather large cavity."

Bagshaw and Ladds (1974) examined 521 bulls at slaughter and reported that "True bulbourethral cysts, encountered in six bulls, were greater than 0.5 cm in diameter and usually contained an opalescent viscid fluid. Of four cysts examined histologically, one was associated with inflammation. The cysts were lined by pseudostratified (1), low cuboidal (2), or columnar (1) epithelium, and were sometimes surrounded by a fibrous capsule."

Bagshaw and Ladds (1974) reported bulbourethral duct dilations in 71 bulls in which the excretory ducts of the glands were greater than 2 mm in diameter: "These dilations were single or multiple, and were scattered throughout the gland; on probing, a duct leading out of them was always found. Usually they contained little or no secretion. Histologically, these dilations were surrounded by a minimal amount of fibrous tissue and were lined by low or high columnar epithelium resembling that of the normal gland."

Metaplastic and cystic lesions of the bulbourethral glands (Fig. 17.4) occur in wethers kept on certain clover pastures whose plants *(Trifolium subterraneum, T. protense, T. repens)* possess high estrogenic potency. Bennetts (1946) stated that "although rams bred and maintained on affected properties have not been found to show any clinical abnormalities, wethers on the other hand commonly show marked teat development and lactation and other abnormalities," including cystic distention of the ducts of the bulbourethral glands. Androgen produced by intact males appears to protect them against the development of squamous metaplasia.

The signs of this estrogenic disease included loss of condition, tucked up abdomen, and frequent bleating "followed by the appearance of a fluctuating swelling below the anus which may develop to such an extent that there is a prominent bulging of the whole perineal region. In some cases a bilateral swelling is present. The swelling is caused by the presence in the pelvic canal of a sac developed on the dorsal aspect of the pelvic urethra with which it communicates and thus become filled with urine" (Bennetts, 1946). Death usually occurred within a few weeks after the cul-de-sac development was noticed. Apparently death was due to toxemia and infection. The cul-de-sac ruptured in some cases and allowed urine to escape through a fistula in the perineum. Following rupture the affected animals survived and improved in condition.

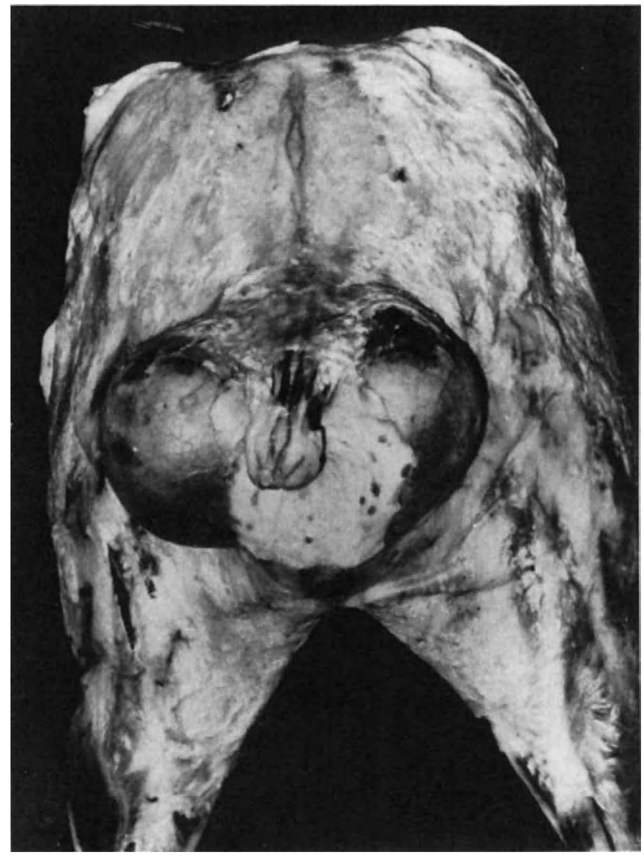

Fig. 17.4. Cystic bulbourethral glands from a wether poisoned by photoestrogens. Acc. No. 10292. (From McEntee, 1970. Photo provided by M. E. Nairn, Perth, Western Australia.)

The histologic lesions consisted of squamous metaplasia of the bulbourethral and prostate glands. "In both organs glandular as well as duct epithelium was highly metaplastic. Other susceptible and commonly affected tissues were the terminal portions of the vasa deferentia, urethral glands of Littré, and the urethra at the colliculus and caudal to this. The vesiculae seminales were entirely unaffected except for the terminal parts of the ducts and no changes were observed in the vesicular remnants of the Müllerian ducts" (Bennetts, 1946). The lesions were identical to those encountered in males of various species subjected to prolonged experimental administration of estrogens.

Bennetts (1947) found that only a few weeks' grazing on "potent green clover" was sufficient to produce profound metaplastic lesions in the accessory reproductive organs. The lesions regressed after the sheep were removed from the offending green clover pasture.

Cook and Shaw (1961) reported that "Elbogen's autopsy series in 1886, indicating 2.3 per cent cystic anomalies of Cowper's duct, still stands as the only anatomical dissection of this area on a large series of human males. If his statistics are correct, more of these anomalies should be seen but there is a paucity of these cases in the literature."

Vesicular Gland

Dilatation of scattered acini occurs in some aged bulls. I have seen a paramesonephric duct cyst on the surface of the right vesicular gland of a 6-year-old bull.

Heller and Whitesel (1963) reviewed the literature concerning cysts of the vesicular gland in seven men and reported two additional cases. They stressed that anatomical authentication is important because true vesicular cysts can easily be confused with cysts arising from paramesonephric and mesonephric remnants. The lesion in a vesicular gland cyst consists of "a wall of collagenous connective tissue with varying amounts of inflammatory reaction, lined with stratified cuboidal to low cuboidal epithelium. The lumen contains amber, non-odorous to foul-smelling bloody fluid with spermatozoa." The incidence of cysts is probably higher than reported because they are frequently small and asymptomatic.

Prostate Gland

Periprostatic Lymphatic Cysts. Periprostatic cysts of the lymphatics are present occasionally in long-standing cases of prostatic hyperplasia in aged dogs. Bloom (1954) stated that "the outer surface of the gland is covered with few or many, round, oval or irregular, thin-walled, translucent cysts which contain a clear watery fluid. The cysts project above the surface and may vary from 2 mm to 3 cm in size. Microscopically, they are enveloped by a thin fibrous capsule and are lined with flattened endothelial cells. The lumens contain a pale eosinophilic homogeneous or granular material."

Periprostatic Cysts Lined by Fibrous Tissue and/or Epithelium. One or more large cysts are occasionally present on the surface of the canine prostate gland, especially in middle-aged and old animals. Some of the cysts communicate, through a relatively small opening, with the prostatic acini and ducts. When multiple cysts are present, fluid may be forced from one cyst into another in some cases. The cysts contain cloudy or brown blood-tinged fluid and fibrin is often present. Some of the cysts are lined by prostatic epithelium and others by fibrous connective tissue. Osteoid tissue is often present in the wall of the large cysts. The cysts may originate from prostatic ducts and alveoli, serosal epithelium, or large hematomas.

Weaver (1978) reported a series of 12 large cysts adjacent to the prostate in the dog. The dogs were 5 to 12 years of age with a mean age of 8.5 years and they had signs of constipation and/or dysuria. They did not have a febrile reaction nor pain on palpation of the prostate and cyst. Weaver did not establish the origin of the cysts but concluded that they did not originate from the paramesonephric ducts. He stated that "The content of the cysts varied from colourless, pink or red serous material through a grey or cloudy appearance to a dark brown viscid material containing necrotic debris. In all instances bacteriological culture, both aerobic and anaerobic, proved that the material was sterile."

Prostatic Epithelial Cysts. Epithelial cysts within the prostate gland (Fig. 17.5) are associated with hyperplasia in the gland of mature and aged dogs. The cysts may become very large (Fig. 17.6) in young dogs that are treated with estrogens for a prolonged period of time and have consequently developed squamous metaplasia of the ducts and alveoli.

Paramesonephric Duct Cyst (Cystic Uterus Masculinus). Paramesonephric duct cysts are usually small in domestic mammals. They are located between the ampullae of the deferent ducts as well as along the more proximal portions of the reproductive ductal system of the male. They are a fairly common incidental finding in most species of domestic mammals. Pinegger (1975) reported a large uterus masculinus that was removed surgically from a 7-year-old dog. The cyst originated from the dorsal aspect of the neck of the bladder and communicated with its lumen. It weighed 560 g and contained approximately

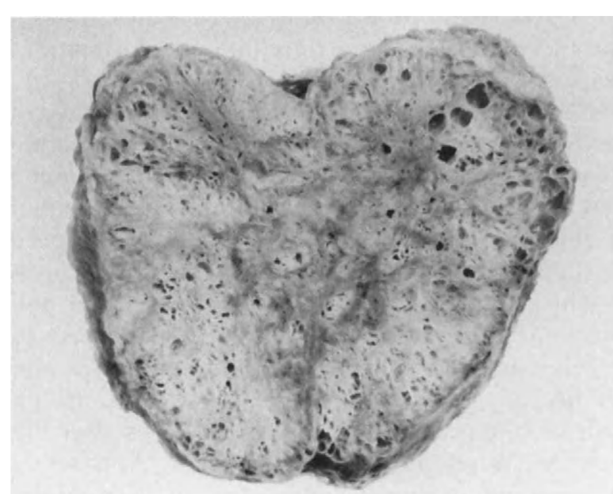

Fig. 17.5. Cross section of a cystic prostate gland from a 16-year-old English Setter dog. The gland weighed 77 g. Acc. No. 1357 (From McEntee, 1970.)

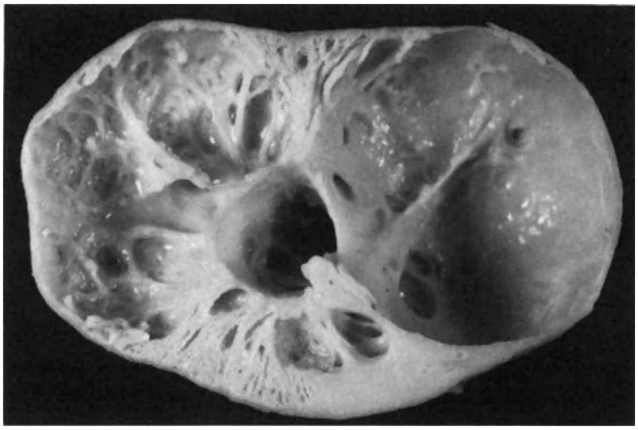

Fig. 17.6. Cross section of a cystic prostrate from a 25-week old dog. Lesion was induced by long-term estrogen administration. Acc. No. 18363.

400 ml of yellow fluid with a urine odor. The cyst was lined by stratified squamous epithelium and covered by smooth muscle and fibrous tissue.

Concretions in the Vesicular Glands

Bagshaw and Ladds (1974a) reported the presence of concretions in the vesicular glands in 11 of 521 bulls from Australia: "The concretions were up to 1.5 cm in diameter, irregular, friable and externally rough. When incised some concretions had a distinctly laminated appearance. Histologically, they consisted of amorphous eosinophilic debris with occasional clumps of enmeshed nuclear material. In all but one bull, the concretions were associated with a mild to severe seminal vesiculitis." The composition of the calculi was not mentioned.

Prostatic Crystals

I have seen crystals in the prostate gland of aged rams. The affected alveoli were enlarged and distorted.

Prostatic Corpora Amylacea

Smith and Chir (1966) emphasized that it is important to distinguish between corpora amylacea and prostatic calculi. They stated that "A corpus amylaceium is a spherical noncalcified body that can vary considerably in size. In section it has a series of concentric layers which stain with different intensities. A calculus consists of one or more corpora amylacea which have become calcified. Calculi may or may not have a regular outline." Corpora amylacea are common in man and the rabbit but are rare in domestic mammals. I have seen them in the prostate gland of a few aged dogs.

Prostatic Calculi

Prostatic calculi are common in man and rare in domestic mammals. Lumb (1952) reported a case of prostatic calculi in a 6-year-old Cocker Spaniel dog. The animal was listless for several days and had difficulty urinating. Radiographs revealed the presence of numerous calculi in the prostate. Exploratory surgery revealed that about three-fourths of the right lobe of the prostate was occupied by a large cyst containing calculi. Another cyst, containing calculi, was found in the left prostatic lobe. The contents of the cysts and the cyst walls were removed surgically.

Lumb (1952) stated that "The two prostatic cysts contained a total of 35 smooth, discoid calculi. They were white, mottled, and streaked with brown, and moderately hard. The largest measured 10 mm in diameter. On qualitative analysis, they were found to be composed of triple phosphates and alkaline earths with probably some admixture of urates." Histologic examination of the cyst walls revealed squamous metaplasia of the cyst lining and infiltration of the connective tissue by lymphocytes, plasma cells, and macrophages.

I have seen prostatic calculi in three aged dogs.

Calcification of the Prostate Gland

Aughey and Weaver (1977) recorded a case of calcification and osseous metaplasia of the prostatic stromal tissue in a 13-year-old Laborador dog. The animal had severe bilateral hip dysplasia and an enlarged prostate. No abnormalities were found on blood and urine examination. The prostate weighed 57 g and measured 5 × 3 × 3 cm. They stated that "the histologic picture is consistent with benign hyperplasia in the increase in the stroma, the cystic dilation of a number of acini, and local areas of inflammation marked by cellular infiltration." The description and illustrations of the epithelial lining of the prostate are those of atrophy.

Inflammatory Lesions

Inflammatory lesions of the reproductive organs are most common in the vesicular glands of ruminants, swine and horses and in the prostate gland of the dog. Epididymitis is frequently secondary to vesiculitis in those species with vesicular glands and secondary to prostatitis in the dog.

Vesiculitis (Seminal Vesiculitis) in the Bull

Lagerlöf *et al.* (1942) mentioned that infectious diseases of the accessory sex glands of the bull were often overlooked. They stated that "In the European textbooks in this field (Richter, Hetzel among others), the diseases of the seminal vesicles are not mentioned at all. The first one to become interested in this question was apparently W. L. Williams who described certain diseases in bulls in his work on "The Diseases of the Genital Organs of Domestic Animals" in 1921."

Most of the reports in the literature dealing with vesiculitis in domestic mammals are concerned with the condition in bulls. Mild cases of vesiculitis, which do not result in marked changes in the glands, are usually overlooked unless the tissue is examined histologically. My experience indicates that vesiculitis is much more common, especially in sexually mature young bulls, than is indicated in most literature reports.

The diagnosis of the specific causes of vesiculitis in the live bull has been difficult in the past because samples collected either by an artificial vagina or a urethral catheter were often contaminated. Parsonson *et al.* (1971) devised a simple and rapid technique for collecting seminal fluids from live bulls for microbiological examination. No bacterial contamination was present in 154 of 158 samples collected by this procedure. The technique is described in detail in their report.

Bacterial Infection. ***Tuberculosis.*** Schlegel (1924) described tuberculous lesions of the vesicular glands of the bull and steer. He stated that the disease is the predominant cause of inflammation of the bovine vesicular gland.

According to Lagerlöf *et al.* (1942), however, tuberculosis is not a major cause of vesiculitis in the bull. They reported the clinical signs of the disease in the genital organs of two bulls. A 4-year-old bull showed signs of illness for 4 days. It had anorexia, laid down most of the time, and groaned while defecating and urinating. Upon examination per rectum the vesicular glands were found to be enlarged, firm, and grown together. The inguinal lymph nodes were enlarged considerably. Following slaughter the bull was found to have pulmonary and peritoneal tuberculosis as well as bilateral tubercular vesiculitis. The left vesicular gland was 18 cm long, 10 cm wide, and 8 cm thick. The right vesicular gland was 18 cm long, 4 cm wide, and 3 cm thick. The cut surface of the glands had partly calcified caseous areas. The testes and epididymides were normal.

The second case occurred in a 2-year-old bull that had served a number of heifers that were reported to have become pregnant. The bull was found to have a greatly enlarged, firm, nonpainful right testis. The bull served willingly and was found to have lumps in the semen. The number of sperm was normal but the motility was decreased. Inoculation of semen into guinea pigs produced tuberculosis and the bull was slaughtered. The bull had diffuse tuberculosis of the lungs, liver, pleura, peritoneum, vesicular glands, and the right testis.

The lesions of tubercular vesiculitis may be unilateral or bilateral and the affected glands are often greatly enlarged. The glands may contain numerous caseous miliary nodules or the entire gland may be converted into a large sac filled with cheesy material. Adhesions are frequently present between the vesicular glands and the adjacent tissue. With the control and elimination of bovine tuberculosis in many parts of the world its importance as a cause of vesiculitis has been greatly diminished.

Mycobacterium paratuberculosis Infection. Larsen and Kopecky (1970) reported the isolation of *Mycobacterium paratuberculosis* from the reproductive organs of six bulls with clinical signs of alimentary canal disease and unthriftiness. The organism was isolated from the vesicular glands of all six animals, from the prostate gland of three bulls, and from the bulbourethral gland of one bull. Although *M. paratuberculosis* is frequently present in the reproductive tract it does not produce inflammatory lesions in these organs.

Brucellosis. Lambert *et al.* (1963) described the lesions in the reproductive organs of two bulls that had been infected with the field strain of *Brucella abortus* for 2 and 5 years. The organism was isolated repeatedly from the semen of both bulls. At necropsy, *Brucella abortus* was isolated from the testes, epididymides, vesicular glands, and ampullae. Both bulls had chronic vesiculitis consisting of numerous interstitial foci of lymphocytes and plasma cells and an increase in the interstitial fibrous tissue.

Lambert *et al.* (1964) reported the reproductive tract lesions in a bull that had been vaccinated with strain 19 of *Brucella abortus* at 5 months of age. Eight months following vaccination the *Brucella* seroagglutination titer was +400 and an organism indistinguishable from strain 19 was isolated from the semen. The bull was killed 12 months postvaccination and strain 19-like organisms were isolated from the vesicular glands, prostate gland, and epididymides. The genital organs appeared normal on gross examination. Histologic examination revealed the presence of chronic interstitial lymphocytic ampullitis and vesiculitis. The epididymides, prostate, and testes appeared to be normal.

According to Lagerlöf *et al.* (1942), orchitis and epididymitis occur more frequently than vesiculitis in

Brucella-infected bulls. They reported the occurrence of abscesses in chronically infected vesicles. They stated that the organism can be demonstrated in the vesicular glands for only a relatively short time and their abscesses may not contain *Brucella abortus*.

Actinobacillus pyogenes (Corynebacterium pyogenes) Infection. *Actinobacillus pyogenes* is the most frequently diagnosed cause of severe chronic vesiculitis in bulls from areas free of brucellosis.

McEntee (1962) reported the isolation of *Actinobacillus pyogenes* from the vesicular glands of 5 of 16 bulls with vesiculitis. *Proteus mirabilis* and *Streptococcus bovis* were each isolated from single cases. Six of 12 bulls, which were examined following slaughter, had concurrent lesions in other parts of the body, suggesting that the infection of the vesicular glands may be metastatic in many cases. The extragenital lesions included traumatic gastritis, chronic pneumonia, pyelonephritis, polyarthritis, endocarditis, and urethral calculi. Blom and Christensen (1965) described the vesicular gland lesions found in six bulls that were infected by *Actinobacillus pyogenes*. Pronounced periglandular inflammation was a prominent feature of the disease. Two of the bulls had adhesion of the vesicular gland to the rectum and a fistular opening to the rectal lumen. The periglandular inflammation was less severe in the other four bulls. Necrosis and sequestration of glandular tissue, with marked abscess formation, was present in three bulls. *Actinobacillus pyogenes* was isolated from the semen of one bull, from the vesicular glands of another bull, and from both the semen and vesicular glands of the other four bulls.

Blom (1979a) reported the postmortem findings in the reproductive organs of 24 bulls with vesiculitis. He stated that the signs of vesiculitis are "more pronounced in acute than in chronic phases of the inflammation. Typical signs are small ejaculates, pink or brownish colour, possibly floccules or lumps of pus, in some cases buttermilk consistency, or even in rare cases complete sedimentation." Neutrophils are abundant in the semen in early stages of the disease but tend to decrease in more chronic cases. Blom found pus cells in the semen in 30 of 32 cases of vesiculitis. The admixture of leukocytes varied from one or a few cells per low-power field to numerous cells that practically obscured the sperm cells. Lesions were not found in the testes nor epididymides. *Actinobacillus pyogenes* was isolated from 8 of the 24 cases examined postmortem. These cases represented the more severe form of the disease with large abscesses, perivesiculitis, and often adhesion to the surrounding tissues. Navel infection during calfhood had occurred in three of these cases. *Escherichia coli* was isolated from the vesicular glands of two bulls. The lesions were not as severe in these cases. Ureaplasma was cultured from the vesicular glands of two bulls, in one case alone and in the other in association with *Actinobacillus pyogenes*.

Miscellaneous Bacterial Infections. Other bacteria that have been reported to cause vesiculitis in bulls include *Actinobacillus actinoides* (Jones *et al.*, 1964), *Corynebacterium renale* (Galloway, 1964), *Pseudomonas aeruginosa* (van der Kaay, 1949), staphylococci (Roberts, 1986), and streptococci (Lagerlöf *et al.*, 1942). These miscellaneous infections of the vesicular glands do not generally result in as much enlargement of the glands as occurs with tuberculosis, brucellosis, and *Actinobacillus pyogenes* infection.

Candidiasis. Mészáros *et al.* (1976) reported the occurrence of vesiculitis, epididymitis, and testicular degeneration in bulls infected by *Candida guilliermondii*. The disease occurred in 51 bulls in three artificial insemination stations. The penis and scrotum became reddened and the penis tended to bleed. The signs did not subside following intravenous treatment with 6 mg/kg of tetracycline per day for 4 to 5 days.

A heavy concentration of yeast cells, identified as *C. guilliermondii*, was found in the semen. Excretion of this fungus was maximal during the acute stage of vesiculitis and decreased markedly during the chronic stage of the disease. The straw bedding at one A.I center and the beet cube ration at the other two stations were "massively contaminated by *C. guilliermondii*." The enzootic mycosis stopped after elimination of the contaminated straw and fodder.

Six of the affected bulls developed aspermia and were slaughtered. Mészáros *et al.* (1976) stated that "the seminal vesicles showed complete adhesion with the surrounding tissues, and in two-thirds of the vesicles studied, the lobular structure was poorly defined. Connective tissue, pushing the glandular tissue away, was visible on the cut surface. Staining by the PAS and Grocott's techniques revealed the presence of yeast cells in the glandular tissue and lumen of the seminal vesicle." Yeast cells were also seen in the testis, epididymis, spleen, pancreas, and lymph nodes.

Chlamydial Infection. Storz *et al.* (1968) reported the isolation of chlamydial agents from the testis and epididymis of two bulls with vesiculitis. Eugster *et al.* (1971) inoculated one bull and five rams with bovine and ovine chlamydial agents. The animals were slaughtered 8 to 22 days after inoculation. Chlamydial agents were isolated from the testes, epididymides, ampullae, vesicular glands, and prostate glands. The animals had interstitial granulomatous lesions in the testes, epididymides, and ampullae of the ductus deferents.

Mycoplasmal Infection. ***Mycoplasma bovigenitalium.*** Blom and Ernø (1967) reported the isolation of *Mycoplasma* spp. from semen containing pus from a 1-year-old bull. Two 19-month-old bulls were experimentally infected with the isolate. The organism was injected into the vesicu-lar glands of one bull and into the left testis of the other bull. Inflammatory lesions developed in the inoculated organs and *Mycoplasma* spp. were isolated from them following slaughter. The organism was identified subsequently as *M. bovigenitalium* (Ernø, 1969).

Al-Aubaida *et al.* (1972) reported a field case and two experimentally induced cases of bovine vesiculitis and epididymitis caused by *M. bovigenitalium.* The field case occurred in a yearling bull owned by an artificial insemination cooperative. Numerous neutrophils were in the semen and the left vesicular gland was enlarged and firm. The enlarged gland was removed surgically. *Mycoplasma bovigenitalium* was isolated from the gland and attempts to isolate bacteria, viruses, and chlamydia were unsuccessful. Diffuse and focal accumulations of lymphocytes, macrophages, and plasma cells were present in the interstitial tissue of the infected gland. Some alveoli contained neutrophils and cellular debris. The bull was slaughtered 4 months following removal of the left vesicular gland. The right gland had a few areas of lymphocytic and plasma cell infiltration around alveoli that contained cellular debris. Most of the sections of the vesicular gland appeared to be normal. Inflammatory lesions were present in the small arteries in the tail of left epididymis. The prostate and bulbourethral glands appeared normal. *Mycoplasma bovigenitalium* was isolated from ampullae, epididymides, kidneys, spleen, and liver but not from the right vesicular gland.

The organism that was isolated from the field case of vesiculitis was used to infect two bulls experimentally. Three milliliters of a broth culture containing approximately 10^5 organisms per milliliter was injected into the right vesicular gland of both bulls. The bulls were slaughtered 11 days later and were found to have vesiculitis similar to that in the field case. Both had inflammatory lesions in the epididymides, ampullae, and prostate glands. *Mycoplasma bovigenitalium* was isolated from the right vesicular gland and deferent duct of one bull and from both vesicular glands, deferent ducts, and epididymides of the other bull. It was not recovered from the testis, kidney, spleen, liver, or lung.

Parsonson *et al.* (1974) reported the results of inoculating *M. bovigenitalium* into the vesicular glands of 13 bulls: "Inflammatory cells were present in the semen of 7 bulls from day 8 post inoculation until slaughter up to 17 weeks post inoculation. *M. bovigenitalium* was isolated from the genital tract of all inoculated bulls at slaughter and from the right carpal joint of one bull." All bulls had vesiculitis and 10 of the 13 had epididymitis.

Hall and McEntee (1981) reported the occurrence of reduced postthawing survival of sperm from bulls with mild mycoplasmal vesiculitis. No other clinical signs of disease were evident. They stated that "In otherwise acceptable semen from young bulls (10 to 18 months old), sperm failed to survive freezing satisfactorily when mycoplasma infection was present in the vesicular glands though there were no clinical signs of vesiculitis. In post mortem examinations of many of these and other young bulls culled for other reasons, foci of mononuclear cells, consisting predominantly of lymphocytes, were present in the vesicular glands." This was due to *M. bovigenitalium* infection.

Mycoplasma bovis. La Faunce and McEntee (1982) reported the occurrence of vesiculitis in bulls following the injection of cultures of *Mycoplasma bovis* into the vesicular glands. They stated that "The infection was characterized by an initial outpouring of neutrophils into the glandular alveoli followed by a marked interstitial response involving macrophages, lymphocytes and plasma cells. However, even in chronically infected glands, areas of acute inflammation characterized by invasion of neutrophils and eosinophils were present in many lobules. . . . Once the infection was established, the organism was shed consistently in all post-infection seminal vesicular secretion samples."

Ureaplasmal Infection. Waelchli-Suter *et al.* (1982) reported the results of injecting cultures of a ureaplasma strain directly into the vesicular glands of bulls. Ten of 11 inoculated bulls developed vesiculitis. They stated that "Based on the findings of this study it can be concluded that the ureaplasma strain used has pathogenic potential for the bovine seminal vesicle. It can cause seminal vesiculitis if inoculated directly into the gland at a dose of approximately 10^9 c.f.u. Based on this study no conclusions can be made as to the role of ureaplasmas in field cases of bovine seminal vesiculitis."

Viral Infection. The evidence that viral infection causes vesiculitis in bulls is weak. Florent *et al.* (1962) isolated a cytopathogenic virus from three bulls with clinical signs of orchitis and from two bulls with vesiculitis. They reported that the virus caused degeneration of the germinal epithelium in experimental bulls. Bögel *et al.* (1963) identified the agent as the G-UP virus. They inoculated 14 calves with the virus and failed to produce disease. They did not mention the route of inoculation.

Maré and Van Rensburg (1961) isolated a virus from bulls with the so-called "epi-vag" syndrome. They reported that the virus was serologically similar to the IBR–IPV virus but had different cultural and cytopathic characteristics. It produced vesiculitis when inoculated into the urethra and epididymitis when injected into the epididymitis.

Vesiculitis in Other Domestic Mammals

Ram. Vesiculitis in the ram has been overlooked by most investigators. Infection of the genital organs of the ram is usually referred to as epididymitis, however, vesiculitis, as in the bull, occurs more frequently than epididymitis. Jansen (1980b) examined the entire genitourinary tracts from 100 rams that were slaughtered because of palpable lesions of the external genitalia, the presence of neutrophils and bacteria in the semen, and/or poor breeding performance. "Only rams from flocks that had been regularly vaccinated against *Br. ovis* infection were selected for study and they were furthermore tested for the absence of *Br. ovis* infection by a cultural examination of their semen. . . . In some of the rams either one or both vesiculae seminales were enlarged and had exaggerated lobulated appearance. In many rams the vesiculae seminales and ampullae appeared normal in spite of the isolation of bacteria from them" (Jansen, 1980b). Although a variety of bacterial organisms were isolated from the reproductive organs, *Pasteurella haemolytica* was recovered most frequently (Jansen, 1980a). The incidence of inflammatory lesions in the genitalia of the 100 rams was: sheath, 79; ampulla, 63; vesicular gland, 60; epididymis, 42; and testis, 28. A similar frequency of vesiculitis probably occurs in rams and goats with brucellosis.

Boar. De Keyser *et al.* (1962) reported that the vesicular gland appears to be the main site of localization of *Brucella suis* in the boar. They also isolated the organism from the prostate gland, bulbourethral gland, epididymis, and urine.

Deyoe (1967) infected swine with *Brucella suis* via the conjunctival route. Gross lesions attributable to *B. suis* infection were present mainly in the vesicular glands and regional lymph nodes. "In general, affected seminal vesicles were yellowish, slightly smaller than usual, firm, and contained multiple focal abscesses, each about 1 mm in diameter." One boar had a greatly enlarged vesicular gland (10 cm in diameter) that was distended with purulent exudate. "Even though orchitis is often cited as a common clinical manifestation of brucellosis in boars, reports of clinical orchitis in numerous boars in a single herd are uncommon."

Stallion. Aamdal and Bøhler (1955) reported a case of decreased fertility associated with chronic inflammation of the vesicular glands and prostate in a stallion. A β-haemolytic staphylococcus was isolated from the infected glands.

van der Holst (1976) recorded the isolation of a pure culture of *Streptococcus equisimilis* from the ejaculates of two stallions with clinical signs of vesiculitis. It was stated that the stallions recovered spontaneously.

Blanchard *et al.* (1988) described a case of vesiculitis and ampullitis, due to *Pseudomonas aeruginosa*, in an 8-year-old stallion. "Two mares that had been bred to the horse by natural service subsequently developed a *Pseudomonas aeruginosa*-related endometritis." A pure growth of the organism had been isolated from the semen of the stallion during the previous breeding season. Treatment of the infection with gentamicin and amikacin failed to eliminate the infection, thus the stallion was killed. *Pseudomonas aeruginosa* was isolated from both vesicular glands but not from other locations. The authors suggested "that negligible amounts of gentamycin diffused across the mucosal cell borders of the accessory sex glands into the seminal plasma. Thus, even though the organism remained susceptible to gentamycin and amikacin *in vitro*, the infection persisted *in vivo*."

The histologic lesions consisted of "superficial infiltration of neutrophils and lymphocytes in the mucosa and scattered, infrequent granulomas in the submucosa of each seminal vesicle. A widespread diffuse infiltration with neutrophils, lymphocytes, and plasma cells was observed in the mucosa and submucosa of each ampulla, along with overlying purulent debris in the lumen" (Blanchard *et al.*, 1988).

Sperm Granulomas. I have seen sperm granulomas in the vesicular glands of the ram. These lesions probably develop following retrograde ejaculation of sperm.

Prostatitis

Prostatitis occurs in all species of domestic mammals but is of clinical significance mainly in the dog (Fig. 17.7). The condition is commonly associated with prostatic hyperplasia in older dogs. Predisposing causes include sustentacular cell neoplasms and estrogen administration. The causes of canine prostatitis include *Escherichia coli*, *Proteus* spp., *Pseudomonas* spp., *Brucella canis*, *Mycobacterium* spp., staphylococci, streptococci, distemper virus, and *Blastomyces dermati-*

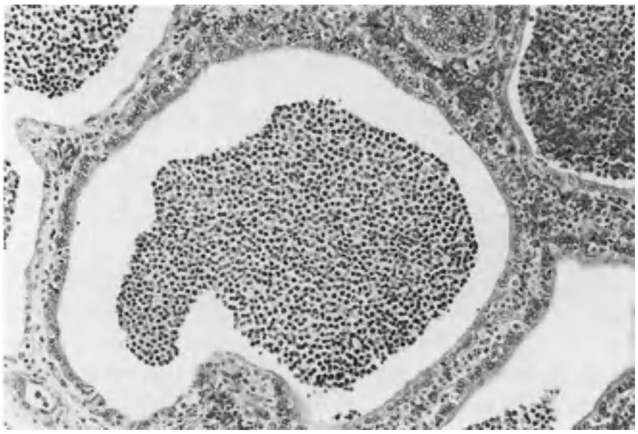

Fig. 17.7. Suppurative inflammation of the prostrate gland from a 7-year-old dog. (Photo by Dr. Leon Z. Saunders.)

tidis. Prostatic abscesses occur when prostatic cysts become infected.

Barsanti and Finco (1984) reported the results of examining 56 cases of prostatic disease in dogs. Prostatic tissue was collected for histologic examination, either by caudal celiotomy and wedge biopsy or at necropsy, from all the dogs. Twenty-five had prostatitis, 22 had prostatic hyperplasia, and 10 had prostatic neoplasia. Abscesses were present in 15 dogs. Bacteria were isolated from prostatic tissue from 20 of the dogs with prostatitis but from none with prostatic hyperplasia. The diagnosis in the other 5 cases was based on the presence of purulent inflammatory lesions in prostatic tissue. They stated that "Blood leukocyte counts were normal in all 22 dogs with prostatic hyperplasia. Leukocytosis, a left shift, or toxic neutrophils were found in 9 of 15 dogs with abscessation, 2 of 10 dogs with chronic bacterial prostatitis, and 2 of 10 dogs with prostatic neoplasia."

Sperm Granulomas. Wu (1982) reported the occurrence of sperm granulomas in the prostate gland of the boar. I have seen the lesion in the vesicular glands of the ram.

Bulbourethral Adenitis

Inflammation of the bulbourethral glands may accompany infection of the vesicular glands but appears to be of less importance. König (1962) and Ball *et al.* (1964) reported focal accumulations of lymphocytes and plasma cells in the interstitial tissue and fibrous tissue proliferation in the glands of bulls. Ball *et al.* (1968) described lymphoid follicles in chronically inflamed bovine glands.

Atrophy of Accessory Reproductive Organs

Atrophy of the accessory reproductive organs occurs following castration, estrogenic stimulation, and advanced testicular degeneration. O'Shea (1962) examined the prostate glands of 331 dogs and stated that "It is suggested that the average prostate passes through three phases during life viz. (a) normal growth in the young adult, (b) hyperplastic growth during middle age, (c) senile involution during old age. From about 11 years onwards there is, on average, a steady decline in prostate relative weight and this is regarded as a phase of senile involution, although histological evidence of atrophy may not be seen." He also reported that "Atrophy of the prostate is commonly seen in dogs suffering from canine distemper and diabetes mellitus. Other systemic diseases may also produce atrophy." The atrophic epithelium becomes flattened and basophilic and the acini collapse (Fig. 17.8). The relatively large amount of interglandular fibromuscular tissue gives the gland a very firm consistency.

Huggins and Clark (1940) reported that the administration of small doses of stilbestrol to dogs produced prostatic atrophy. They suggested that the atrophy in response to estrogen may be produced indirectly by depression of pituitary gonadotrophin secretion. This would reduce androgen secretion by the testes and therefore a prostatic atrophy by the lack of androgen.

Metaplasia of Accessory Reproductive Organs

Metaplasia of the accessory reproductive organs of the male occurs in association with chronic inflamma-

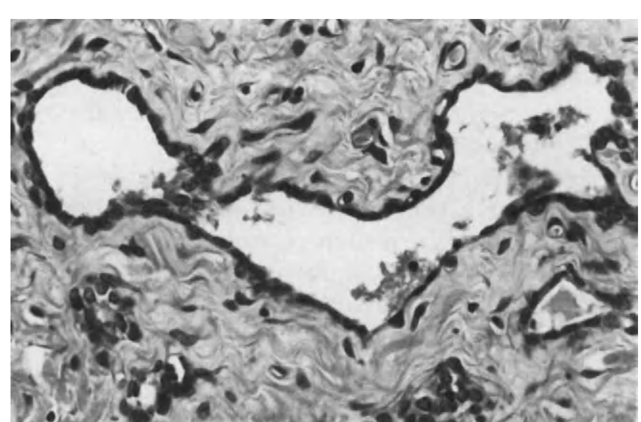

Fig. 17.8. Atrophic canine prostate with acini lined by flattened epithelium. ×355. Acc. No. 17003.

tion of the glands, hyperestrogenism, highly chlorinated naphthalene poisoning, and zeranol (a derivative of zearalenone) implantation.

Zuckerman and Groome (1937) described squamous metaplasia of the prostate gland of dogs with sustentacular cell tumors of the testis and those treated with estrogens. Cotchin (1960) and O'Shea (1963b) reported squamous metaplasia of the prostate in dogs with interstitial cell tumors, suggesting that some of these neoplasms may produce estrogen. Inflammatory lesions are common in glands with squamous metaplasia. Metaplasia regresses following removal of the testicular neoplasms except in cases in which they have metastasized.

Squamous metaplasia of the prostate and bulbourethral glands of sheep is discussed in this chapter in association with cysts.

McEntee and Olafson (1953) reported the occurrence of squamous metaplasia of the epididymis and accessory reproductive organs (Fig. 17.9) of bulls that were poisoned by highly chlorinated naphthalene. Metaplasia did not occur in the reproductive organs of the poisoned ram. The disease was originally known as hyperkeratosis (X disease).

Wu (1982) reported osseous metaplasia of the bulbourethral glands of the boar.

Hyperplasia of Accessory Reproductive Organs

Hyperplasia of the accessory reproductive organs is of little significance except in the canine prostate gland. It is the most common pathologic condition in the prostate of the dog and it may cause rectal and/or urinary obstruction. Focal areas of hyperplasia may be present in an otherwise atrophic gland (Fig. 17.10).

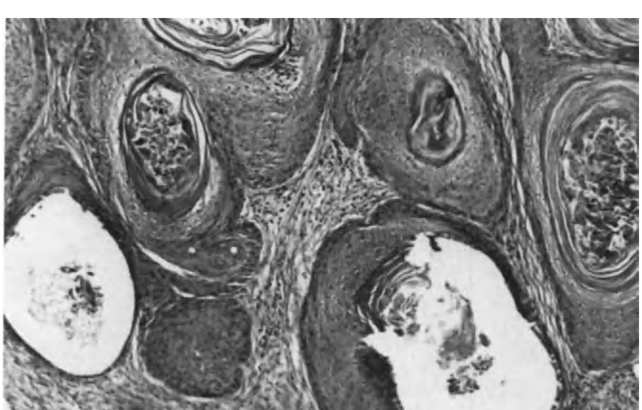

Fig. 17.9. Squamous metaplasia of the bovine vesicular gland due to highly chlorinated naphthalene poisoning. ×89. Acc. No. 466.

Fig. 17.10. Atrophic prostate with focal area of hyperplasia from a 7-year-old dog. ×56. Acc. No. 14277.

O'Shea (1962) reported the results of postmortem examination of the prostate glands of 331 dogs. Three hundred were unselected dogs and 31 were selected because of prostatic or testicular abnormalities. He stated that "although growth of the prostate in the adult dog appears to proceed at a fairly steady rate up to about 11 years, the histological structure does not remain constant. During the period from about 3 to 6 years of age, the normal histological structure is frequently lost and the onset of glandular hyperplasia is seen." He found that the relative weight of the prostate of the Scottish Terrier was "approximately four times as great as the mean prostatic weight of all other adult dogs." However, only 1 of 10 Scottish Terriers had difficulty defecating and urinating.

A gradual transition occurs from normal glandular tissue to hyperplastic epithelium. O'Shea (1962) stated that "In hyperplasia, large, irregular-shaped alveoli, often exceeding 500μ in diameter, with numerous and often branching infoldings of their epithelium, are seen. The columnar cells are sometimes taller than normal (hypertrophy) and their cytoplasm may be more deeply eosinophilic, but these are not constant features. Alveoli exceeding 500μ in diameter, and lacking infoldings of their epithelium, are regarded as cysts."

James and Heywood (1979) examined the prostate glands of 198 Beagle dogs that were between 37 weeks and 7.75 years of age. The weight of the glands increased markedly with advancing age. They found that 84.4% of the youngest dogs had prostate glands weighing less than 5 g and all the glands in this group weighed less than 10 g. Among the oldest dogs less than 5% of the glands weighed less than 10 g whereas over 50% exceeded 20 g.

De Klerk *et al.* (1979) stated that spontaneous hyperplasia of the canine prostate appears to progress with age from a glandular to a cystic hyperplasia.

They reported that "Prostatic hyperplasia can be induced in young beagles with intact testes by treatment for 4 mo with either dihydrotestosterone or 5α-androstane-3α, 17β-diol, alone, or with either of these steroids in combination with 17β-estradiol. In contrast, the induction of prostatic hyperplasia in young castrated beagles, in which the gland had been allowed to involute for 1 month, requires the administration of both 17β-estradiol and either 5α-androstane-3α, 17β-diol or dihydrotestosterone. Testosterone and 17β-estradiol, either singly or in combination, did not produce the hyperplastic condition in intact or castrated beagles." Cystic hyperplasia of the prostate was not produced in young dogs by any of the treatments. They stated that "cystic hyperplasia is characterized by a cuboidal but hyperplastic epithelium, with the formation of large cysts, and an increase in the ratio of stromal to epithelial cells. Occasionally prostates are seen in various stages that appear to represent transition from glandular to cystic hyperplasia. Glandular hyperplasia may represent an early stage of development of the disease preceding the appearance of cystic hyperplasia."

Brendler *et al.* (1983) conducted a study of spontaneous prostatic hyperplasia in 42 Beagle dogs that ranged in age from 8 months to 9 years. They found that the prostate enlarges for at least 6 years, whereas the ejaculate volume and total ejaculate protein decline markedly after 4 years of age. They stated that "these reciprocal growth and functional changes in the prostate are closely associated with a progressive increase in the incidence of BPH (benign prostatic hyperplasia), which is already apparent in some dogs by age two. With age there is a modest decrease in serum androgen levels with no apparent changes in serum 17β-estradiol levels. This suggests that the growth and functional changes that are associated with the development of BPH and are initiated very early in life reflect an altered sensitivity of the prostate to serum androgens or a response to the relative decrease in the serum androgen to estrogen ratio."

Neoplasia of Accessory Reproductive Organs

Epithelial neoplasms of the accessory reproductive organs occur mainly in the canine prostate gland and are extremely rare or nonexistent in the other species of domestic mammals. Prostatic tumors do not occur as frequently in the dog as they do in man. Epithelial neoplasms that metastasize to the prostate are seldom reported. Carcinomas of the urinary bladder sometimes invade the prostate. Connective tissue neoplasms occur occasionally in the accessory reproductive organs.

Kotz (1958) reported a 1252 g leiomyosarcoma of the prostate gland of a dog. The dog developed hydronephrosis and uremia due to occlusion of the urethra and right ureter. The neoplasm contained areas of hemorrhage, necrosis, and calcification. Metastatic lesions were present in the peritoneum, mesentery, liver, urinary bladder, ureters, spermatic cords, and testes.

I have examined the following canine prostatic neoplasms: 17 carcinomas, 1 adenoma (Fig.17.11), 2 lymphomas, 1 fibrosarcoma, 1 leiomyoma, and 1 hemangioma.

Woolridge (1912) reported an adenoma of the prostate from a 14-year-old Fox Terrier. The dog had a poor appetite and was losing weight when it was presented for examination. Clinical examination revealed that the dog was emaciated and had pale mucous membranes. A large, hard mass was palpated in the front of the pubis. Exploratory laparatomy revealed that the mass was a greatly enlarged prostate. Death occurred 2 days following surgery. The lesion was diagnosed as a prostatic adenoma on the basis of histologic examination. The lesion was not described nor illustrated.

Hornbuckle *et al.* (1978) conducted a retrospective review of 140 randomly selected cases of prostatic disease in the dog. Uncomplicated cases of prostatic hyperplasia were not included because this is such a common condition in the dog. They found 22 cases of prostatic adenocarcinomas. The neoplasms occurred in dogs from 5 to 13 years of age and the average age was 9.9 years.

Grant (1957) reviewed the literature concerning prostatic carcinomas in the dog and presented a detailed description of two cases. He stated that "it seems reasonable to conclude that carcinoma of the canine prostate is a distinct, often highly malignant

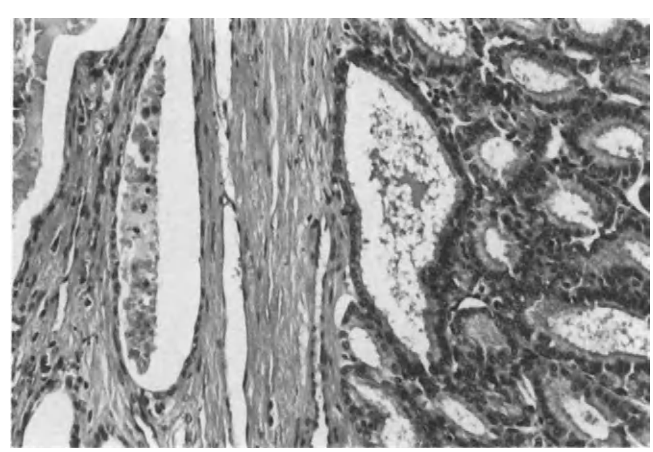

Fig. 17.11. Adenoma in an atrophic prostate of a 12-year-old dog. ×178. Acc. No. 16796.

and widely metastasising neoplasm of low frequency which occurs independently of alterations in the balance of sex hormones and the associated changes in the prostate."

Weiss (1962) found 13 cases of prostatic carcinoma in a series of 1680 dogs that were examined after death. There were five undifferentiated adenocarcinomas, five solid carcinomas, two simple adenocarinomas, and one squamous cell carcinoma. Metastases were present in adjacent organs and lymph nodes in all cases and in the lungs, heart, and kidneys in 11 dogs. Bone metastases were not found.

Leib *et al.* (1986) reported a squamous cell carcinoma of the prostate gland of a 5-year-old English Springer Spaniel. The dog had "multiple limb lameness which was caused by diffuse bone pain." The dog was killed because of progressive clinical signs of bone disease. "The prostate gland measured 3 cm by 4 cm and was asymmetrical due to greater enlargement of the right side of the gland, which was soft, fluctuant, and contained a 2 cm abscess with thick green, purulent material. Iliac lymph nodes were not enlarged but contained areas of focal necrosis and several white nodules 1 mm to 3 mm in size" (Leib *et al.*, 1986). Necropsy revealed the presence of metastases of the neoplasm in the iliac lymph nodes and in the right scapula, right humerus, right radius and ulna, both femurs, and all the lumbar vertebrae.

O'Shea (1963a) reported six cases of adenocarcinoma and one case of a transitional cell carcinoma of the canine prostate gland. The latter tumor appeared to arise from the prostatic urethra. Mucoid secretory material was observed in all the neoplasms.

Leav and Ling (1968) studied 20 cases of adenocarcinoma of the canine prostate. The material was collected at necropsy over an 11-year period at Angell Memorial Hospital, Boston, during 1956–1967. The dogs ranged in age between 6 and 15 years, and the mean was 10.1 years. There was no breed predilection. They stated that "The most frequent clinical signs were emaciation, rear limb weakness, lumbar pain, straining to defecate, straining to urinate, polydipsia and polyuria. In many cases, rear limb locomotor disturbance was the major presenting sign. In others straining to defecate or to urinate predominated." Sixty-five percent of the dogs were emaciated.

Leav and Ling (1968) classified adenocarcinomas of the canine prostate into "two broad types: (A) those which formed acini or alveoli were designated *adenocarcinomas,* and (B) those which did not form these structures were classified *undifferentiated adenocarcinomas.* The *adenocarcinomas* were further divided into two types: type one—*intra-alveolar proliferative* (Fig.17.12), and type two—*small acinar.* The *undifferentiated adenocarcinomas* were also divided into two types: type three—*syncytial type* (Fig.17.13), and type four—*discrete epithelial type.*" Variations in the dominant pattern were frequent within the same gland and metastastic foci usually resembled the histologic pattern present in the primary site.

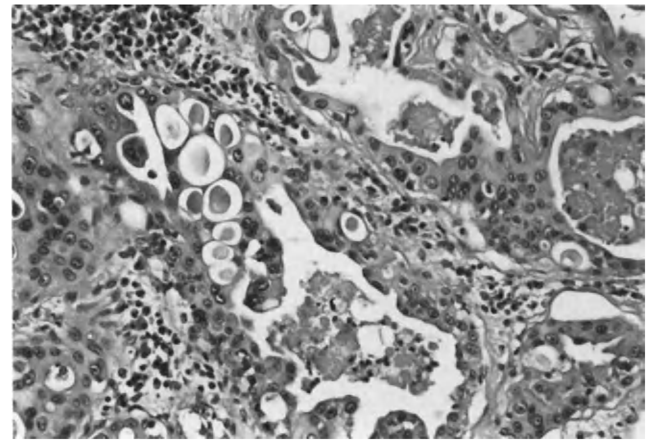

Fig. 17.12. Intraalveolar proliferative carcinoma of the prostate of a 10-year-old dog. × 178. Acc. No. 14598.

Metastatic lesions were found in 15 dogs in the external and internal iliac lymph nodes, which were firm and enlarged. The lungs contained metastatic foci in 13 animals. The incidence of metastatic lesions in other organs included: urinary bladder, 10 dogs; bone, 7; omentum and mesentery, 7; rectum, 6; pelvic muscle, 5; heart, 5; adrenal, 2; kidney, 2; spleen, 2; and liver, 1. They stated that the skeletal metastases "may not be discovered unless careful radiographic studies are done and the vertebral columns and pelves of all suspected cases are examined at necropsy. Foci of neoplastic cells in areas of skeletal metastasis were surrounded by dense fields of fibrosis, bone destruction, and new bone formation" (Leav and Ling, 1968).

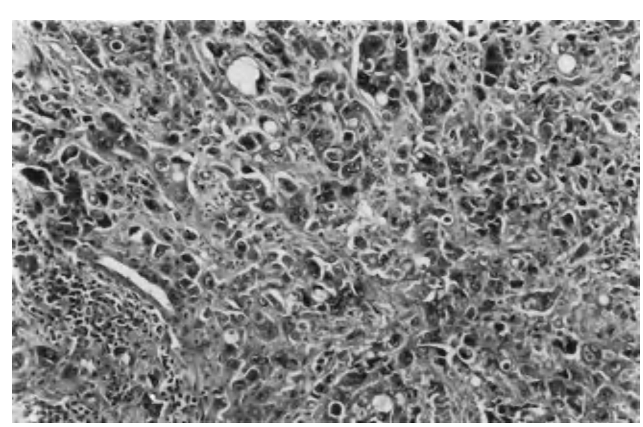

Fig. 17.13. Syncytial prostatic carcinoma from a 9-year-old dog. ×89. Acc. No. 4389.

Goedegebuure (1979) reported skeletal metastases in three of nine dogs with prostatic adenocarcinomas. It was stated that "as in man prostatic carcinomas had a predilection for the vertebral column." Batson (1940), Franks (1953), and Leav and Ling (1968) have reported that the vertebral venous system offers a path of spread of prostatic carcinoma to the pelvis, the femora, and the vertebral bodies. Franks stated that "Batson suggested, and the present work supports his view, that if the inferior vena cava is obstructed in life by increased intra-abdominal pressure due to straining, coughing, etc., the blood flow may be diverted into the vertebral venous system, carrying with it tumour or other emboli." Leav and Ling concurred with this view and stated that a predominant entering complaint by the owners of 20 affected dogs was that the animals strained to defecate.

Durham and Dietz (1986) reported the signalment, clinical signs, and histologic tumor pattern of 12 dogs with prostatic carcinoma. Five (42%) of the dogs were found to have skeletal metastases of the neoplasm. "Weight loss and lumbar pain were observed more frequently in dogs having prostatic adenocarcinoma with metastases to bone." The incidence of bone lesions may have been higher than reported because three of the dogs "were not radiographed at the common site of metastasis to bone, the pelvis and lumbar spine." It was also mentioned that early metastastic lesions in bone can occur without radiographed evidence of metastases. Metastatic lesions in extrapelvic bone included the scapulas, ribs and digits.

Alsaker and Stevens (1977) reported a case of peripheral blood invasion of a prostatic carcinoma in a 6-year-old dog. The neoplastic cells in the blood had delicate chromatin, increased nuclear to cytoplasmic ratio, and cellular pleomorphism. They stated that these cells could be mistaken for large lymphocytes or monocytes.

Evans *et al.* (1985) reported a prostatic carcinoma in a 7 1/2-year-old dog that had been castrated 5 1/2 years earlier. They referred to other reported cases of carcinoma of the prostate in castrated dogs. They stated that "It is not clear whether there is a sparing effect on the risk of prostatic adenocarcinoma in male dogs neutered at an early age, as has been shown in the bitch relative to mammary cancer."

Gill (1981) reported a prostatic adenocarcinoma with a concurrent sustentacular cell tumor in a 13-year-old dog. The photomicrograph of the testicular neoplasm appears to be that of an interstitial cell tumor rather than a sustentacular cell tumor.

Hargis and Miller (1983) reported 14 cases of prostatic carcinoma in dogs that averaged 8.5 years of age. Seven of the dogs had been castrated for up to 5 years before the tumors were diagnosed. They stated that the "Clinical signs varied markedly but were usually related to the urinary tract. The most common signs included prostatic enlargement in seven dogs, hematuria, stranguria, or tenesmus in four dogs, and neurologic signs relating to rear-leg weakness in three dogs. Duration of signs varied from two weeks to four years." Ten of the cases were diagnosed as adenocarcinoma and four as undifferentiated carcinoma.

I have seen one carcinoma of the prostate gland of a 4-year 9-month-old cat, which had been constipated for about 3 weeks. The diameter of the pelvic cavity was decreased and exploratory laparotomy revealed a soft tissue mass in the pelvic inlet. The cat died while recovering from anesthesia. The prostate consisted of tubules, cords, and nests of anaplastic epithelial cells. Numerous neutrophils and lymphocytes were scattered throughout the neoplasm. Metastatic lesions were not found. Cotchin (1984) reported a fibroadenoma of the prostate of a 13-year-old cat.

Mostofi and Leestma (1971) reported that benign neoplasms of the human prostate are rare and that carcinomas "constitute the second most frequent cause of deaths from cancer in the male population of the United States. . . . Carcinoma of the prostate gland is found unexpectedly and incidentally in 26% to 37% of autopsy examinations of patients who have died from some other cause, and by the ninth decade the figures are 40% to 80%."

Although prostatic carcinoma is common in man, it is negligible as a cause of death in the dog and is practically nonexistent in other domestic mammals.

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Chapter 18

Penis and Prepuce

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Bibliography

Anatomic Features

The book by Schummer, Nickel, and Sack (1979) is recommended for a description of the anatomy of the penis and prepuce of domestic mammals. The penis is fused to the prepuce in sexually immature domestic mammals. Bharadwaj and Calhoun (1961) referred to the fused area as the balanopreputial fold. They reported that "the pattern of the fold differs in most animals. It is smoothly circular in the boar, ventrally interrupted in the dog, and sends off 'secondary' folds in the region of the processus urethrae in the young male sheep and goat."

Ruminants

The urethral process of young lambs and goats is embedded in, and adherent to, the preputial mucous membrane. Belonje (1965) reported that the fusion persists when lambs are castrated at 3 to 6 weeks of age but there is complete separation of the penis and prepuce when they are castrated at 4 months of age.

In adult rams and buck goats the urethral process appears to have the function of spreading semen around the cervix at the time of copulation. Gunn (1936) stated that in the ram "when well-marked erection occurs and when the ejaculum is voluminous, there have been noticed very definite movements of the urethral process, the free end of which rapidly describes a circle forming a cone, the apex of which is its attachment to the glans penis. The effect is a very complete scattering of the ejaculate, which, at a distance of 1 foot, may spread over nearly a square yard if the penis is held in the open."

Ashdown (1962b) reported that separation between the penis and sheath in cattle "commenced at about 3 or 4 months and was completed at about 9 or 10 months. Great differences were, however, found between animals of similar ages." These variations are due to different rates of growth associated with breed differences and nutritional condition.

The relaxed penis forms an S-shaped curve (sigmoid flexure) that is located between the thighs and is medial to the spermatic cords. The erect penis of the mature bull is 80–110 cm long; that of the adult ram and buck goat is 30–50 cm in length. The penis of *Bos indicus* bulls is somewhat longer than that of the *Bos taurus* breeds. During erection and service the bovine penis protrudes 25 to 60 cm out of the prepuce. Schummer *et al.* (1979) stated that the "Retraction of the penis does not depend on the action of the retractor penis muscle. It is brought about largely by the return of elastic elements in the proximal curve of the flexure which has been tensed during erection." This explains why massive calcification of the retractor penis muscle of the bull does not interfere with retraction of the penis.

The terminal 2 to 3 cm of the bovine urethra forms "the urethral process which is visible in a groove on the right side of the tip of the penis. The external urethral orifice is a narrow slit in the papilliform end of the process. Because the orifice is small, urination is slow and takes place in squirts rather than in a continuous flow" (Schummer *et al.* 1969). The urethral process of the ram and buck goat projects beyond the glans penis for about 3 to 4 cm and becomes smaller toward its end.

The bovine prepuce is 25–40 cm long and the relaxed penis occupies the caudal third of the sheath. Lymphoid nodules are present in the preputial mucosa of all domestic ruminants.

Hinkle *et al.* (1978) were unable to pass a catheter into the urinary bladder of male goats because of the presence of a urethral diverticulum (recess) located dorsal to the pelvic portion of the urethra. They stated that "considering the anatomic relationships involved, catheterization of the male goat urethra may be contraindicated. The urethra at the point of the diverticulum is not only reduced in diameter but also collapsed, unless the animal is urinating. . . . Catheterization attempts may cause unnecessary trauma, resulting in necrosis and scar formation."

Garrett (1987) reported that the structure that was described by Hinkle *et al.* as a diverticulum should be "designated as the urethral recess, because it has a large mouth or opening, in contrast to a diverticulum, which has a small opening." He examined the urethral recess from 14 male goats, 1 bull, 3 steers, 2 boars, 1 ram, and 4 wethers. "In all ruminant specimens, an oval recess was found extending caudodorsally to the urethra at the junction of its pelvic and spongy parts. In the goats and the sheep, the recess was 0.5 cm deep; it was 1.5 cm deep in the steers and the bull. . . . The urethral recess in the porcine genital tracts formed a hemispheric space projecting dorsocaudally from the junction of the pelvic and spongy parts of the urethra. The depth of the recess, measured from the opening of the pelvic part, was 1.25 cm in the 90-kg boar and 0.5 cm in the 9-kg boar." In regard to the possible function of the urethral recess Garrett stated that "the fold of mucous membrane containing the termination of the ducts of the bulbourethral glands may act as a check valve to prevent backflow into the pelvic part of the urethra and, thus, aid in the expulsion of urine or semen in those animals having a long penis with a small diameter urethra."

Stallion

The equine penis contains a large amount of erectile tissue and is about 50 cm long in the quiescent state in the mature horse. According to Schummer *et al.* (1979), "the part of the penis becoming visible at erection is about 30–50 cm long and has a diameter of 5–6 cm." The horse has a more prominent glans penis than the other domestic mammals. "It caps the distal end of the corpus cavernosum and has a circular edge, corona glandis, proximal to which is a constriction, collum glandis. At the front is the fossa glandis which contains the urethral process." The urethral sinus or diverticulum is located dorsal to the urethral process. The diverticulum sometimes becomes filled with inspissated smegma. The penis of the stallion does not have a sigmoid flexure.

Boar

The cranial portion of the porcine penis has a small glans that is spirally twisted counterclockwise. Schummer *et al.* (1979) stated that "the penis of the pig belongs to the fibroelastic type and when erect resembles a thin, tapering stick about 60 cm. long. In cross section it is dorsoventrally flattened proximally, round at the middle, and laterally flattened at the tip."

The boar has a prominent preputial diverticulum that is located dorsal to the preputial os and contains urine, semen, desquamated epithelial cells, and occasionally concretions. The diverticulum is surgically removed from boars that are used for artificial insemination to reduce the bacterial content of the semen. Aamdal *et al.* (1958) stated that "the diverticulum is pear-shaped and has a distinct neck which opens into the prepuce, approximately 3 to 4 cm caudal from the preputial orifice. The opening varies in size but usually will admit one or two fingers. The caudal and widest part of the diverticulum is divided by a longitudinal septum into a pouch on each side, dorsal to the prepuce."

Dog

The dog has an os penis that develops after birth and is considered to be an ossified portion of the corpora cavernosa. The bone is grooved ventrally for passage of the urethra. The glans penis consists of the bulbis glandis, the proximal one-third of the glans, and the pars longa glandis, the distal or cranial two-thirds of the glans. The bulbis glandis expands during coitus and prevents withdrawal of the penis from the vestibule of the bitch during ejaculation. During coitus the dog dismounts and faces in the opposite direction. This is considered to be a protective position because the dog has a prolonged ejaculation time.

Fisher (1917) reported that "The retractor penis muscle in the dog is a cord-like structure, pale and translucent in its anterior portion but somewhat darker and more fleshy in its posterior portion." He found that the fibers in the anterior three-fifths of the muscle were wholly smooth while in the posterior two-fifths the fibers were both smooth and cross-striated. One-third to one-half of the fibers in the caudal portion were found to be striated.

Cat

Schummer *et al.* (1979) stated that "The short penis of the cat has retained its original embryonic orientation and is directed caudoventrally." Ives *et al.* (1975) reported that the penile spines (papillae), which are present in mature intact tom cats are first seen between 9 and 13 weeks of age and their eruption and growth are completed after 8 months. The cat has approximately 100 to 120 of these structures, which regress following castration and reappear under androgen therapy.

According to Jackson (1902) an os penis is rarely found in the cat "except in old animals and occurs as an ossification within the distal prolongation of the septum between the corpora cavernosa." The os penis is about 3 to 5 mm long. Abundant adipose tissue is present in the corpora cavernosa penis.

Anomalies

Aplasia of the Penis

Absence of the penis is rare in otherwise normal animals. It sometimes occurs in association with hermaphroditism and with other defects in the genital system.

Absence of Preputial Orifice

Elam and Randle (1952) reported the absence of a normal preputial opening in a 5-week-old mongrel puppy. A preputial tuft of hair was also missing. The preputial cavity became distended with urine and it oozed from minute pores in the prepuce. Death occurred when urine production exceeded elimination. According to the owner, two other puppies in the litter and one of a previous litter of five had the same preputial defect.

Hypoplasia of Preputial Orifice (Phimosis and Paraphimosis)

A congenitally small preputial orifice may prevent protrusion of the penis (phimosis) or return of the penis into the sheath (paraphimosis) when the penis becomes distended after protrusion. Chaffee and Knecht (1975) reported a case of paraphimosis in a 4-year-old Poodle with a 2-year history of prolonged intermittent penile protrusion as a result of inefficient preputial muscles. The clinical condition was corrected by surgically shortening the preputial muscles.

Hypospadias

Hypospadias is a condition in which the external orifice of the urethra is located on the ventral aspect of the penis at any location between the normal opening and the ischial arch. There may be single or multiple openings or the entire urethra may fail to close.

Ader and Hobson (1978) reviewed the literature on hypospadias in domestic mammals and reported three additional canine cases. They stated that "In its most severe form the penis is short and the glans penis is small. A deep cleft lined with mucous membrane occurs on the ventrum of the penis, and the urethra opens in the perineal region. The scrotum remains separated into two halves, each of which contains a testicle. In lesser grades of hypospadias the scrotal halves are joined and the penis is larger, but a part of the urethra remains open ventrally and the opening is more posterior than usual." They classified hypospadias as glandular, penile, scrotal, and perineal. In the perineal form the penis is located so as to resemble a vulva.

Hypospadias has been reported to occur in the bull (Robles, 1930; Raust, 1939; Wollrab and Rechenberg, 1964), ram (McFarland, 1958; Noice and Schipper, 1958; Gilanpour, 1971; Dennis, 1979), goat (Eaton, 1943), boar (Langpap, 1962), and dog (Croshaw and Brodey, 1960; McFarland and Deniz, 1961; Kipnis, 1974).

Epispadias

Epispadias is a malformation in which the urethra opens on the dorsum of the penis. It occurs much less frequently in domestic mammals than hypospadias.

Diphallus (Double or Bifid Penis)

Diphallus is a rare congenital anomaly. Roberts (1943) described a case that occurred in a Holstein bull. A single bladder opened into two urethrae. Prostatic tissue was located on the left urethra but was not found on the right urethra. The two urethrae entered the base of the penis, which was single until distal to the S-shaped curve, where it divided into two. Urination took place through both urethrae while ejaculation occurred only through the left urethra and penis.

Bosu and Barker (1971) reported a case of diphallus in a 15-month-old Holstein bull that was unable to breed because the penis protruded only 2 to 3 inches on attempted copulation. The urethra was duplicated from the glans to the base of the penis. The other reproductive organs were normal.

I saw a case of diphallus in a young Holstein bull that was being used for artificial insemination in Brazil. I was not able to follow the case to see if he transmitted the condition to his sons.

Supernumerary Ectopic Penis

Wolfe *et al.* (1987) described a supernumerary penis that occurred in the right paralumbar fossa of a Beefmaster calf. They reported that on clinical examination at 1 month of age "The haired tubular growth was 30 cm long and 4 cm in diameter and appeared to be a sheath containing a penis-like structure. Otherwise the calf appeared normal." The structure was removed surgically and was found to contain a corpus penis cavernosum surrounded by tunica albuginea. "A normal corpus spongiosum penis and urethra terminated proximally at an internal prostate gland. The haired portion of the structure was surrounded by skin and muscle consistent with the penile sheath of a normal bull." The incision healed without complication and when the bull was examined at 15 months of age, "Rectal palpation indicated that the bull had normal internal genitalia and a 2-cm circumscribed area of fibrous tissue at the ventral border of the medial aspect of the wing of the right ileum. A palpable association between the excised ectopic tissue and the primary urogenital tract was not found."

Micropenis

Micropenis is an unusually small penis. Bloom (1954) reported that the condition occurs most frequently in Great Dane, Collie, and Dachshund dogs. The condition is common in hermaphrodites and pseudohermaphrodites of all species of domestic mammals.

Megalopenis

Megalopenis refers to an unusually large penis. According to Bloom it occurs in certain toy breeds of dogs, especially in the Ray Pinscher, Chihuahua, and Pekingese. These breeds have a penis that is disproportionally large in relation to their body size.

Persistent Penile Frenulum

The frenulum is a band of epithelial-covered dense connective tissue on the ventral midline of the penis. Following separation of the penis and prepuce during puberty a portion of the frenulum may persist (Fig. 18.1) and interfere with the ability of the animal to copulate.

Ashdown (1962c) reviewed the literature concern-

Fig. 18.1. Persistence of two portions of the penile frenulum of an Aberdeen Angus bull. Acc.No. 18282.

ing the occurrence of the defect in bulls and reported four additional bovine cases. He suggested that the "frenulum is predisposed to persistence at points where it is transversed by a large blood vessel."

Carroll *et al.* (1963, 1964) reported that Aberdeen Angus and Beef Shorthorn bulls were most commonly affected. Five of eight affected Hereford bulls were from an intensely inbred herd. They reported that the defect was most likely inherited by transmission of a recessive gene. Elmore *et al.* (1978) found that 6 of 18 related Angus bulls from one farm had persistence of the penile frenulum. Dozza (1956) reported the occurrence of the defect in 15 young Chianina bulls.

Aamdal and Nes (1958) reported persistence of the penile frenulum in five related Norwegian Landrace boars. They suggested that the condition was inherited but the mode of inheritance was not determined.

Persistence of the penile frenulum has been reported in the following breeds of dogs: Miniature Poodle (Joshua, 1962; Belkin, 1969; Hutchison, 1973), Pekingese (Begg, 1963), and Cocker Spaniel (Hutchison, 1973; Ryer, 1979; Balke, 1981). The condition in the dog is probably much more common than the literature indicates because many male dogs are not used for breeding. Pernial defects in these cases are frequently overlooked.

Detached Urethral Process

Saunders and Ladds (1978) examined four bulls with detachment of the urethral process, which gave the free end of the penis a bifid appearance. Three of the bulls were from one herd.

Deviations of the Penis

Seidel and Foote (1967, 1969) used a clear lucite tube connected to an artificial vagina to photograph the ejaculation process in a number of bulls. The process was recorded at 64 frames per second. Twisting of the penis was observed in more than half of the ejaculations, ranging from a slight twist to a 360° counterclockwise coil. The length of extension of the penis from the entrance to the artificial vagina averaged 53 cm.

Spiral deviation of the penis that occurs before intromission is known colloquially as "corkscrew penis." Ashdown and Pearson (1973b) studied the condition in 27 bulls of which 14 were Herefords and 11 of these were polled. One of the horned Herefords sired hornless progeny out of Friesian cows. The other affected breeds included Jersey, Aberdeen Angus, Charolais, Friesian, Guernsey, and Polled Devon. Most of the bulls had served normally, for varying periods of time, before the condition occurred.

Ventral or rainbow deviation and S-shaped deviation of the penis are less common. Walker (1971) stated that all three types of penile deviation "appear to be due to an insufficiency of the dorsal ligament of the penis." Walker and Vaughan (1980) reported that "With a spiral deviation, the ligament slips off to the left side, often complicated by some separation of the longitudinal fibers of the apical ligament along the right side of the penis. The result is a left-handed corkscrew appearance to the distal end during erection. . . . The ventral deviation occurs when the ligament is thin and stretched to the point where it is incapable of holding up the distal portion of the penis during erection and the rainbow appearance becomes evident. . . . The S-shaped deviation occurs in older bulls with an excessively long penis. The apical ligament is sufficient in strength but insufficient in length, and the S shape is noticed upon erection."

Congenitally Short Penis

Roberts (1986) reported that a congenitally short penis has occurred in the bull, buck goat, boar, and stallion. He stated that the condition has been observed in 20 sons of a Hereford bull and in 2 closely related Guernsey bulls. The other reproductive organs were normal in these animals. Shortening of the penis is of common occurrence in hermaphrodites in all species of domestic mammals.

Membranous Penile Urethra

Kipnis (1974) reported the occurrence of a membranous penile urethra in a Toy Poodle that had had several episodes of hematuria. He stated that "Exteriorization of the penis revealed a blunted penile tip and an external urethral orifice which was recessed approximately 5.0 mm. The urethral orifice was broadened and membranous. The membranous urethra extended 10 mm., at which point it blended with the penile tissue."

Aplasia of the Retractor Muscle of the Prepuce

Long and Hignett (1970) reported absence of the retractor muscle of the prepuce in 10 polled bulls and suggested that preputial eversion in these bulls was related to the absence of the muscle. On the other hand, Larsen and Bellenger (1971) reported that the retractor muscle of the prepuce was present in the cases of prolapse that they examined. They suggested that prolapse of the prepuce in beef bulls is due to an excessively long prepuce.

Aplasia of the Retractor Penis Muscle

Aplasia of the retractor penis muscle appears to be a rare malformation. I have seen only one case of this anomaly. A Holstein-Friesian bull had unilateral absence of a retractor muscle, which did not interfere with retraction of the penis.

Short (Hypoplastic) Retractor Penis Muscle

De Groot and Numans (1946) reported the occurrence of a congenitally short retractor penis muscle as a possible recessive character in Dutch Friesian bulls. The S-shaped curve on the penis failed to straighten during erection. However, the affected bulls were able to protrude the penis following resection of the retractor penis muscle. This procedure was not recommended because it appeared that the defect was transmitted recessively.

Hofmeyr (1967b) reported shortness of the retractor penis muscle in young bulls and also suggested that the condition was a hereditary defect. Shortness of the adnexa of the retractor muscles was mentioned as another cause of erection failure.

Abnormal Venous Drainage of the Corpus Cavernosum Penis

Ashdown *et al.* (1979a) found abnormal venous drainage of the corpus cavernosum penis by the dorsal venous system in six young bulls that had never served successfully. The bulls showed good libido but lacked penile erection. They stated that "Radiography of the cavernous bodies and veins of the penis in the living animal demonstrated major venous drainage of the corpus cavernosum penis (ccp) by the dorsal venous system in all cases. This was not seen in normal bulls. . . . The evidence suggests that abnormal venous drainage of the ccp may have been the immediate cause of impotence in these bulls." The defect appeared to be congenital rather than acquired.

Occlusion of the Longitudinal Canals of the Corpus Cavernosum Penis

Ashdown *et al.* (1979b) reported a lack of penile erection in nine bulls with occlusion of the longitudinal canals of the corpus cavernosum penis. Four were impotent when first put into use and five had previously served successfully. They stated that "In each bull, the dorsal longitudinal canal of the corpus cavernosum penis was occluded by fibrous tissue and this was considered to be the immediate cause of impotence. The ventral canals were also occluded in four bulls." They suggested that the defect in the young bulls may have been of congenital origin.

Congenital Deformity of the Os Penis

Johnston (1965a) reported that the os penis of the dog "may develop with a pronounced curvature, and as a result of this deformity the straight portion of the penis can be retracted, but the curved cranial portion is permanently exposed. The exposed glans becomes dry and fissured, resulting in severe infection and necrosis."

Traumatic Lesions of the Penis and Prepuce

Contusion of the Penis and Prepuce

Contusion of the penis and prepuce may result from accidents in all species of domestic mammals or from the forceful extraction of the canine penis from the vagina during mating.

Laceration of the Penis and Prepuce

Trauma may cause laceration of the penis and prepuce in all species of domestic mammals. Laceration of the penile mucosa occurs in some bulls from which semen is collected for the first time after several years of sexual rest. These are bulls that are withheld from semen collection until their progeny tests have been completed. A combination of vigorous mounting and forceful application of the artificial vagina to the penis results in tearing of the penile mucosa. The tear starts on the raphe penis at the junction of the free part of the penis and the caudal portion of the prepuce and extends dorsally on both sides of the penis (Fig. 18.2). Most of the lacerations extend for about one-half of the distance around the penis and may occasionally involve the entire penile circumference. The lacerations are usually sutured and it takes about 6 weeks for the mucosa to heal to a sufficient degree to allow semen collection without further injury.

Penile and preputial lacerations can occur during natural service. Williams and Hagan (1916–1917) stated that during service "the coital thrust of the bull

Fig. 18.2. Lacerated penis of a 5-year-old bull. Acc.No. 16563.

is vigorous, or even violent. It is so violent that occasionally the prepuce is torn or ruptured."

Johnston (1965a) stated that "wounds on the dorsal aspect of the penis may occur when a dog jumps over wire which catches the top of the prepuce, pushes it back and exposes the penis to trauma. Multiple small puncture wounds to the penis and prepuce may be inflicted during fights."

Hematoma of the Penis (Rupture of Corpus Cavernosum Penis, So-called "Fracture" of the Penis)

Hematoma of the bovine penis results from rupture of the corpus cavernosum penis with hemorrhage into the surrounding tissue. Beckett *et al.* (1974) devised a system for determining the rupture pressure in the penis of bulls following slaughter. They found that "the mean rupture pressure of 25 recently collected bovine penile specimens was 1,486 psi with minimum and maximum of 1,180 and 1,720 psi, respectively. The rupture site in 24 of the 25 specimens was in the dorsal surface of the distal curve of the sigmoid flexure." They mentioned that the experimentally induced pressure "is probably exceeded in the natural rupture because of the sudden (fraction of a second) angulation produced by the force of the weight and momentum of the bull at the time of his thrust and ejaculation. Severe bending or angulation of the penis could possibly weaken the tunica albuginea surrounding the corpus cavernosum penis and lower the pressure to cause rupture."

Knaus (1976) reported a case of extensive hematomas of the penis in a 3-year-old ram. The animal recovered following treatment and was used successfully for breeding.

Pascoe (1971) reported a case of rupture of the corpus cavernosum penis of a 7-year-old stallion and referred to a few other published cases. Pascoe stated that while covering a fractious mare the stallion was "dislodged with full erection and was thought to have been hit somewhere on the penis by one of the sidelines restraining the mare. . . . On the following day a mare was covered and when insertion of the horse's penis had occurred a great gush of blood issued from the mare's vulva," and a 15-mm tear was found in the dorsal portion of the diverticulum of the fossa glandis. "This tear led directly into one of the blood spaces in the corpus cavernosum." The laceration was sutured and upon healing of the wound the stallion was used for breeding with no further penile hemorrhage.

Infarction of the Penis

Ruminants. When semen is collected from a bull with an artificial vagina (AV), care must be taken to ensure that a rubber band, which fastens the liner of the AV to the shell, does not become separated and attached to the free part of the penis. If the loss of the rubber band is not noticed and removed immediately, a portion of the penis will become infarcted. The necrotic portion of the penis will detach in about 10 to 14 days (Fig. 18.3). Infarction of a portion of the bovine penis does not interfere with urination. However, affected bulls can not be used for service because of the loss of sensation in the penis.

Wolfe *et al.* (1983) reported the occurrence of penile hair rings in bulls as a result of homosexual activity. They stated that "Body hair from the bull being ridden accumulates on the penis of the more aggressive bull and forms a firm band when the penis is retracted into the preputial cavity. The hair ring may cause pressure necrosis of the urethra and lead to a urethral fistula. Avascular necrosis and sloughing of the glans penis may occur if the condition goes unnoticed."

Careless or unskillful use of a Burdizzo forceps to castrate animals can cause necrosis of that portion of the penis that is compressed by the instrument. Pearson (1972) reported the inadvertent compression of

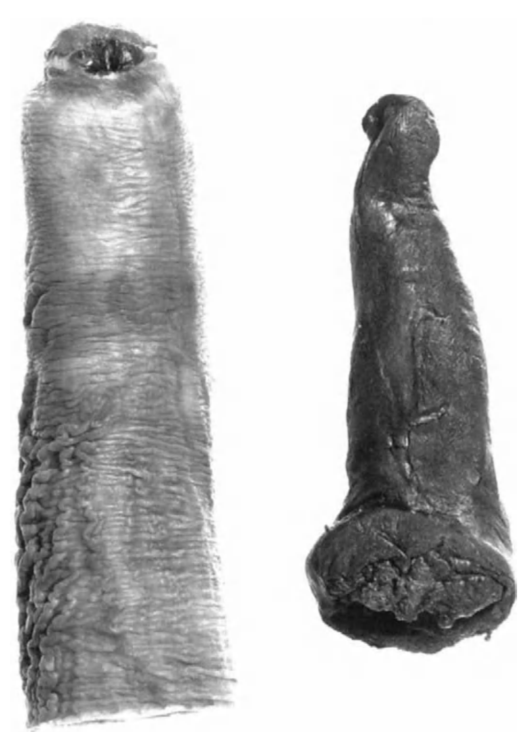

Fig. 18.3. Necrotic portion of a bovine penis and viable remaining part. A rubber band had slipped off an artificial vagina, became attached to the penis, and caused infarction. Acc.No. 802.

the penis in two 6-month-old calves. I have seen several similar cases in lambs.

Dog. Strangulation of the canine penis may occur following the malicious placement of rubber bands around the penis or after the accumulation of preputial hair around the penis. Johnston (1965a) stated that "Swelling, circular necrosis of the penile mucosa, or complete necrosis of the penis distal to the constriction may be evident, depending on the stage of strangulation. When necrosis does not extend through the tunica albuginea, removal of the cause and instillation of an antibiotic in an oily base into the prepuce result in prompt healing. Amputation of the penis is indicated when its distal portion is gangrenous or the urethra is injured so as to interfere indefinitely with urination."

Hair Rings on the Penis

Cat. Hair rings occasionally form around the base of the glans penis in the cat and prevent intromission. Hart and Peterson (1971) stated that "the behavioral pattern which indicates that a penile hair ring may be present is persistent mounting with intense and prolonged pelvic thrusting. Upon retraction of the sheath, hair rings of varying size have been found at the base of the glans." The cat is usually able to complete the mating shortly after removal of the hair ring.

Epidermoid Cysts of the Prepuce

Mosaheb *et al.* (1973) reported epidermoid cysts of the prepuce of Shorthorn and Santa Gertrudis bulls from five herds in Australia. The cysts were usually multiple and were located in preputial skin near the orifice. Most of the cysts were about 3 mm in diameter but some were up to about 1 cm in circumference. The cysts contained a brown doughy material and were lined by stratified squamous epithelium. The etiology of the cysts was not established.

Lloyd (1964) investigated the etiology of epidermoid cysts in Merino sheep in Australia. He concluded that the cysts were due to the implantation of epithelial cells by grass seeds that penetrate the skin.

Fracture of the Os Penis

Fracture of the os penis is a rare condition in the dog. When an adequate history is available it is usually found that the dog injured the penis while attempting to jump over a fence or other barrier. An affected dog has dysuria, usually has hematuria, and exhibits crepitus and pain when the penis is palpated. The penis may angle downward from the middle of the os. The bladder becomes greatly distended with urine. There is usually a single fracture in the central portion of the bone. Johnston (1965b) stated that the fracture "results from severe trauma which often causes additional injury to the penis or prepuce. Fractures are usually transverse and simple with limited soft tissue damage, but may be comminuted with penetration by fragments into the cavernous spaces of the penis, urethra, or the tunica albuginea." Radiography of the penis may be necessary to confirm the diagnosis. The fractured bone compresses and may sever the urethra. The condition may occur in dogs of any age and has been seen in a puppy only 6 weeks old (Denholm, 1957). The fracture is diagnosed in some dogs soon after the injury occurs and the condition is corrected surgically. In others, several months elapse before a diagnosis is established (Bradley, 1985). In the chronic cases the dogs eventually have dysuria and dribble urine from a distended bladder. Surgical correction is much more difficult in chronic cases because of the formation of bone callus on the fractured segments of the os penis.

Exostosis of the Os Penis

Bloom (1954) reported that "small single or multiple exostoses occasionally involve the os penis of the dog. They usually produce no harmful effects, although in some instances there is compression stenosis of the penile urethra." Exostoses may develop in areas of healing fractures of the os penis.

Stenosis of the Prepuce

Stenosis of the preputial orifice (phimosis) may be due to injuries and infections. The lesion occurs most frequently in cattle with a pendulous sheath. It also occurs occasionally in dogs, cats, and stallions.

Hofmeyr (1968a) reported 25 cases of stenosis of the parietal layer of the prepuce excluding the preputial orifice, and remarked that it is one of the most common surgical conditions affecting the penis and adnexa of the bull. The external appearance of the condition was not spectacular. Some edema was noted during the acute stage of the disease. After this subsided the enlargement of the prepuce was so slight that it was easily overlooked. The amount of granulation tissue involved varied from a thin band up to 10 cm of fibrous tissue. It was stated that "not a single case of adhesion of the glans penis to the parietal layer of the prepuce was encountered. It is conceded that adhesions may occur where there has been extensive destruction of both the parietal and penile layers of the prepuce but such occurrences would be exceptional. It is contended that the supposed prevalence of adhesions is erroneous and is based on the confusion between what constitutes adhesion and what stenosis" (Hofmeyr, 1968a).

Prolapse of the Prepuce, Penis, and Urethra

Prolapse (Eversion) of the Preputial Epithelium

Long (1969) reported the incidence of preputial eversion in 244 bulls of British breeds. She stated that "Twenty-eight (85 percent) of 33 polled bulls everted whereas only three (1.4 percent) of 211 horned bulls did so. Eversion occurred concurrently with any activity while bulls were standing, but was especially frequent prior to penile erection, during defaecation and micturation, and at times of particular excitement."

Irreversible Prolapse of the Preputial Epithelium

A pendulous sheath, such as occurs in Angus, Hereford, Santa Gertrudis, Brahman, and Africander bulls, may result in irreversible prolapse of the preputial epithelium. A portion of the penis usually protrudes with the prolapsed prepuce. The condition can be corrected by amputation of the prolapsed part of the prepuce.

Prolapse of the Urethra

Prolapse of the canine urethra occurs infrequently. It may follow infection of the genitourinary tract or excessive sexual excitement. Johnston (1965a) stated that "When the mucosa has prolapsed, congestion and swelling of the everted portion occur, resulting in an irreducible mass." The prolapsed tissue becomes dark red and bleeds intermittently.

Sinibaldi and Green (1973) reported that "A history of dribbling urine with frank blood, frequent urination, sexual excitement, intermittent erections, and the small "red pea" mass at the tip of the penis are all signs of urethral prolapse. The condition has occurred primarily in young English bulldogs between 9 and 13 months of age, which may indicate a predisposing congenital or genetic defect." They stated that five of the six reported cases were in English bulldogs.

Paralysis and Prolapse of the Penis

Rabies can cause paralysis and prolapse of the penis in the bull, stallion, and dog and probably in other species of domestic mammals. Horses develop penile paralysis during the late stages of dourine.

In regard to paralysis of the penis Bloom (1954) stated that "acute cases occur more frequently in puppies than in adult dogs. Any factor that contributes to a cachetic state, such as intestinal parasitism, improper diet, vitamin deficiencies, and debilitating diseases, appears to be causative. Chronic cases are seen in all breeds, perhaps more frequently in small toy breeds. The causes may be trauma, spinal lesions, paraplegia and undetermined."

Wheat (1966) reported the occurrence of prolonged penile paralysis in 10 stallions following the administration of the tranquilizer propriopromazine. He stated that "When the general effects of the drug disappeared, the penis failed to retract into the prepuce. Within 2 days the penis became swollen, and attempts to manually replace it were unsuccessful." In five horses the paralysis existed for 8 months. The stallions had libido but were unable to develop erection of the penis. The penis had reduced sensation to painful stimuli. One horse was used for breeding 2 years after the onset of paralysis but the tip of the penis still protruded from the prepuce. Wheat stated that "Of the total number of horses given injections of propiopromazine, the percentage known to have developed paralysis of the penis is low."

Hurtgen (1983) stated that "Penile paralysis may result from local neurologic damage, rabies and use of phenothiazine tranquilizers. Tranquilizer-induced paralysis of the penis, which has been observed following the use of propiopromazine and acepromazine but not xylaine, results in a seemingly partial erection of the penis. . . . The penis is painful in deep palpation for about two weeks after the onset of paralysis."

Ulceration of the Penile Mucosa

Lein *et al.* (1968) reported ulceration of the penile mucosa of bulls following the local application of dihydrostreptomycin for the treatment of venereal vibriosis. Lesions were observed in 17 of 28 animals that were examined within a week after treatment. Plaques of necrotic epithelium sloughed from the penis (Fig. 18.4) and the mucosa healed within a few days. No permanent adverse effects were noted. One percent acriflavin jelly and lime cause severe necrosis of the penile epithelium.

Adhesions of the Sigmoid Flexure of the Penis

Adhesions sometimes develop in the second bend of the sigmoid flexure of the bovine penis (Fig. 18.5) following the injection of an anesthetic to block the dorsal penile nerve. The bull is unable to protrude the penis after the adhesions form.

Fig. 18.4. Necrosis and sloughing of the penile mucosa of a bull following dihydrostreptomycin treatment on three successive days. The penile mucosa started to slough on the fourth day after the last treatment and the bull was killed on the fifth day. Acc.No. 10983.

Calculi in the Preputial Diverticulum

Calculi occasionally develop in the preputial diverticulum of the boar.

Urethral Calculi (Uroliths)

A detailed discussion of urethral calculi in the dog and cat has been presented by Osborne *et al.* (1972). They stated that 60 to 90% of all uroliths in dogs are composed of phosphates, 10% consist of amonium urate, and 5% are composed of ammonia acid cystine. Many uroliths that are predominantly of one type have traces of another type of mineral. Osborne *et al.* reported that cystine uroliths occur exclusively in male dogs, urate uroliths occur more frequently in the male, and phosphate uroliths are present most frequently in the urinary bladder of female dogs. They stated that uroliths occur less frequently in the cat and that most are composed phosphates.

Osborne and Lees (1978a) summarized the information on the etiology of the feline cystitis, urethritis, and urethral obstruction syndrome in the cat. Three viruses (a picornavirus designated Manx calicivirus, a syncytium-forming myxolike virus, and a herpesvirus) have been implicated in the pathogenesis of the syndrome. They stated that "A unique but as yet unidentified protein has been detected in the urine and urethral plugs of male cats with the naturally occurring form of the disease. It was postulated that the viruses may directly or indirectly cause the production of this protein, and that the protein may serve as a matrix to aid conglomeration of struvite crystals." Struvite crystals are composed of magnesium ammonium phosphate hexahydrate. Osborne and Lees (1987a) stated that the "Urethral plugs typically have no structural organization, being composed of unorganized conglomerates of crystals and debris rather

Fig. 18.5. Fibrous adhesions in the second bend of the sigmoid flexure of a bovine penis. Acc.No. 1334.

than the highly organized crystalline nature of classical uroliths."

Urethral calculi usually lodge in the sigmoid flexure of the bovine penis. They may also lodge in this location in the ram and buck goat but they are found more frequently in the urethral process in these species.

Walker (1979a) reported penile calculi to be very common in feedlot steers, in young bulls on a high plane of nutrition, and in range steers in sandy areas. He stated that "The calculi produced in feedlot steers are relatively soft, smooth and often multiple. The calculi in range steers are rough and hard, and contain a high percentage of silicon."

Degeneration of the Retractor Penis Muscle

McEntee (1958) reported the occurrence of necrosis and calcification of the retractor penis muscle (Fig. 18.6) of bulls that were 9 to 16 years of age. The lesion also occurs in younger bulls but the incidence and degree of degeneration increase with age. The degeneration starts in the center of the muscle at the first bend of the sigmoid flexure. Protrusion and retraction of the penis are not affected. The lesion appears to be due to (1) a high calcium intake and (2) stretching of the muscle during erection of the penis. McEntee *et al.* (1980) found a highly significant ($P < 0.001$) decrease in the incidence of the lesion following a reduction of the calcium in the feed.

Phalloposthitis (Penoposthitis, Inflammation of the Penis and Prepuce)

Phallos is the Greek word for penis, *posthe* for prepuce, and *balanos* for glans. Inflammation of the penis and prepuce is usually referred to incorrectly as balanoposthitis, which means inflammation of the glans penis and prepuce and does not include lesions of the free part of the penis. Inflammatory lesions are always present in the free part of the penis when they are present in the glans and prepuce. In fact, no postnatal animal is free of microbial organisms and inflammatory lesions in the mucosa and submucosa of these structures. Thus inflammation of the penis and prepuce is merely a matter of degree and varies according to the involved pathogen. Many bacteria, viruses, fungi, mycoplasma, ureaplasma, chlamydiae, and protozoa are present in the preputial cavity of domestic mammals without producing significant clinical disease.

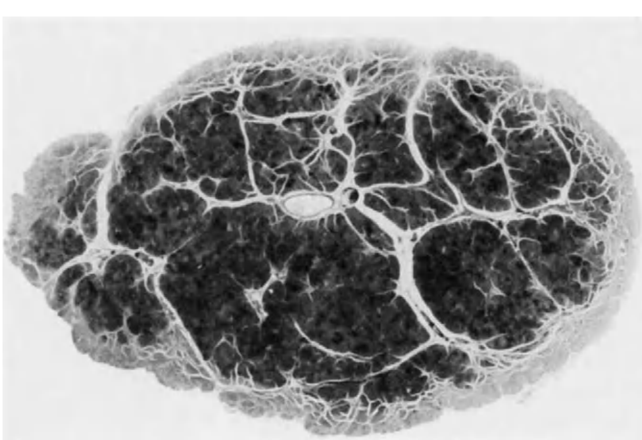

Fig. 18.6. Cross section of a bovine retractor penis muscle with extensive calcification. ×6. Acc.No. 6712.

Bacterial Infection

Bull. The urethra, except for a short distal portion, is free of inflammatory lesions unless the bull has infection of the urinary bladder, the internal accessory reproductive organs, and/or the epididymis and testis. Some sexually mature young bulls develop suppurative phalloposthitis associated with organisms to which older bulls have become resistant. These animals usually recover spontaneously within 10 days to 2 weeks. This condition probably occurs in other species of domestic mammals. Deep penetrating wounds of the sheath result in the development of fistulous tracts that are very difficult to treat successfully.

Campylobacter fetus subsp. venerealis (Vibrio fetus subsp. venerealis). This organism causes endometritis in the cow but no recognizable inflammatory lesions in the reproductive organs of the bull. The bacteria can be found on the sheath of young exposed bulls for short periods of time but persistent infection does not occur until the animal is at least 3 years of age. *Campylobacter fetus* subsp. *venerealis* lives in the epithelial crypts of the penile mucosa. The crypts are not present in young bulls. They are androgen dependent and develop slowly over a long period of time. They reach their maximum size at 5 to 6 years, at which time bulls become infected readily on venereal exposure to infected cows.

Actinomyces pyogenes (Corynebacterium pyogenes). Penile and preputial abscesses in the bull are usually due to infection by *Actinomyces pyogenes.* Penetrating wounds of the penis and/or prepuce generally precede the development of the abscess. Large deep abscesses may interfere with protrusion of the penis.

Corynebacterium renale. Riet Correa *et al.* (1979) reported the occurrence of ulcerative posthitis in 1096 bulls on 17 different properties in Uruguay. The histologic lesions consisted of acanthosis, parakeratosis, and hyperkeratosis followed by invasion of leukocytes in the preputial epithelium. They stated that "Based on the isolation of *C. renale*, histologic lesions and the greater incidence in animals on high planes of nutrition, it is postulated that the lesion is due primarily to production of ammonia following the hydrolization of urea by the organism."

Mycobacterium bovis. Williams and Hagan (1916–1917) and Williams (1918) reported and illustrated the gross penile lesions of tuberculosis in the bull. Williams described a case of penile tuberculosis as follows: "The apex of the glans for a distance of about three inches was much inflamed and enlarged, and bled readily upon touch. The diseased tip was dark livid, the epithelium largely destroyed, and the surface contaminated by purulent exudate." Tubercle bacilli were seen in stained smears of the exudate. He stated that the lesion "is comparatively common in the bull. The corpus cavernosum, urethra, and urethral mucosa are not so frequently involved as the submucosa of the glans, prepuce, sheath and adjacent penial lymphatics."

Dermatophilus congolensis. Infection of the bovine prepuce by *Dermatophilus congolensis* was reported by Mosaheb *et al.* (1973). The condition occurred following a period of heavy rain. "Macroscopically the lesions were raised and up to 5 mm in diameter. The overlying matted hair was readily removed to reveal focal suppuration." The lesions were diagnosed histologically on the basis of finding characteristic gram-positive filaments in the preputial and scrotal skin.

Stallion. The equine penis is frequently washed prior to mating to reduce bacterial contamination of the semen. Swerczek (1979) stated that we have "demonstrated that the penises of stallions washed with disinfectants became infected with potential pathogens such as *Pseudomonas aeruginosa.* It appears that disinfectants actually predispose stallions to pathogenic bacteria."

Bowen *et al.* (1982) also reported that the systematic washing of the stallion's penis caused the normal flora to be replaced with pathogenic bacteria. They stated that cleaning of the penis with "Ivory soap tended to encourage the replacement of the normal flora with coliform organisms, while Betadine favoured the growth of *Pseudomonas aeruginosa* and *Klebsiella* spp."

Wether. Ulcerative posthitis (sheath rot) occurs primarily in castrated sheep and goats but may also occur in intact males. The difference in susceptibility between intact and castrated males appears to be due to the incomplete unfolding of the penis and prepuce in castrated animals and the tendency of the wether to urinate within its sheath.

Ladds (1985) stated that "Development of the primary lesion depends on the occurrence of a transmissible, urea-hydrolyzing bacterium, now considered to be *Corynebacterium renale,* and on the excretion of urine rich in urea. Other factors in urine, possibly hormonal in origin, may also be involved. High protein and especially leguminous diets predispose to the disease, and the incidence is lowest during the summer. It is presumed that wethers are infected by the transmission of material on contaminated bedding, herbage, or by flies."

The lesion usually begins as epidermal necrosis on the dorsal part of the bare tip of the prepuce. The preputial orifice may become occluded by expansion of the lesion. Ladds (1985) reported that "Secondary lesions occur when the prepuce becomes swollen due to the accumulation of urine or pus. At this stage there is more or less extensive internal ulceration of the prepuce (which may slough), destruction of the urethral process, and ulceration of the glans penis."

Boar. Bollwahn and Schoon (1980) described hemorrhagic ulcers of the porcine preputial diverticulum. They stated that the development of the ulcers occurs in association with hyperkeratotic and parakeratotic lesions of unknown cause. The lesions interfere with the breeding ability of affected boars and this is regained following extirpation of the preputial diverticulum.

Dog. Catarrhal inflammation of the penis and prepuce is of common occurrence in the mature dog and is due to a variety of bacteria. *Proteus vulgaris, Escherichia coli,* staphylococci, and streptococci have been isolated from the exudate but the infection is usually due to a mixture of organisms. Johnston (1965a) stated that "When a significant infection develops, the discharge from the prepuce is copious and possibly bloodstained. The lymph nodes beneath the mucosa of the penis and prepuce increase in size, and the mucosa becomes thickened, indurated, and granular. Adhesions may develop between the prepuce and penis, preventing protrusion of the penis."

Viral Infection

Bull. *Bovine Herpesvirus-1 Infection (Bläshenausschlag, Infectious Bovine Rhinotracheitis (IBR), Vesicular Venereal Disease, Coital Exanthema, Exanthema Pustulosum Coitale, Infectious Pustular Balanoposthitis).* Bovine phalloposthitis, due to bovine herpesvirus-1 infection, begins as minute hemorrhagic lesions in the epithelium covering the lymphoid follicles of the penis and prepuce. Necrosis and pustules form in these foci and the lesions erode to form 1- to 3-mm ulcers. Intranuclear inclusion bodies are present in the dying epithelial cells on the edge of the ulcers. The inclusions differ from those that occur in association with equine coital exanthema in that they can be demonstrated only following fixation of the tissue in a hard fixative such as Bouin's solution. The inclusions that occur in the equine disease can be demonstrated in formalin-fixed specimens. The ulcers coalesce into large irregular-shaped areas of necrosis. The lesions heal within about 10 days in uncomplicated cases. However, the affected bull remains infected for life and may shed the virus when subjected to stress. Lesions are not usually evident in the bull at this time and the infection may be spread to susceptible cows by the use of natural service or by artificial insemination with the virus-contaminated semen.

Dennett *et al.* (1976) reported that "Twenty-six (65%) of 40 seropositive bulls shed detectable IBR virus into the prepuce after corticosteroid treatment. . . . No correlation was observed between initial circulating antibody titre and virus excretion after treatment. There were no significant changes in levels of serum antibody during the virus excretion period."

Boeckx *et al.* (1968) reported the spread of the disease to cows by the use of semen from bulls with penoposthitis. They found a significant decrease in the nonreturn rate and a highly significant increase in shortened estrous cycles in cows bred with semen from infected bulls. Practically all bulls in the stud become infected.

Stallion. ***Equine Herpesvirus-3 Infection (Equine Coital Exanthema, Coital Vesicular Exanthema, Genital Horsepox).*** The earliest visible lesions of equine coital exanthema are 2- to 3-mm pustules in the mucosa of the penis and prepuce. Intranuclear inclusion bodies are present in the affected epithelial cells. Ulcers develop and extend to form large areas of epithelial necrosis. The ulcers cause focal areas of depigmentation of the penile and preputial epithelium (Fig. 18.7). The depigmented areas are often the site of squamous cell papillomas and squamous cell carcinomas in old animals.

Molluscum Contagiosum in the Horse. Rahaley and Mueller (1983) reported the occurrence of infection of the prepuce of a stallion with the poxvirus of molluscum contagiosum. Multiple pale, dome-shaped papules, up to 3 mm in diameter, were present on the hairless portion of the prepuce. Similar lesions were present on the muzzle below the nares. Discrete areas of epithelial proliferation with characteristic "molluscum bodies" were located in the epithelium. Rahaley and Mueller stated that these bodies are "brightly eosinophilic, dyskeratotic keratinocytes containing intracytoplasmic pox virions," and are considered to be pathognomonic for the disease. The outcome of the infection was not established because the horse was killed because of cervical vertebral instability (equine "wobbler" syndrome).

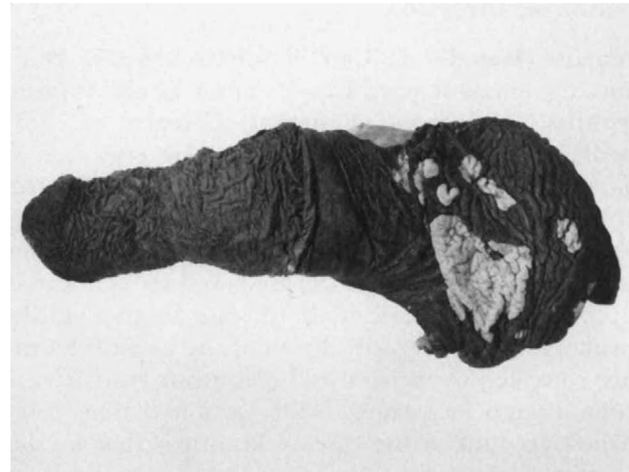

Fig. 18.7. Depigmented areas of the equine penis and prepuce following equine herpes-3 infection. Acc.No. 15283.

Dog. ***Canine Herpesvirus Infection (Dog Pox).*** Hill and Maré (1974) induced infection of the penis and prepuce of four dogs with a suspension of a canine herpesvirus. A serous discharge from the prepuce was noticed 3 to 7 days after inoculation. The hair around the preputial opening was continually wet and the dogs were sensitive to handling of the penis and prepuce. Petechial hemorrhages and inflammatory lesions developed over the base of the penis and on the preputial reflection. Lymphoid follicles developed in these areas. The penile lesions regressed in 4 to 5 days and virus was isolated up to 20 days postinoculation. Intranuclear inclusions were not mentioned, however, Poste and King (1971) found them in infected tissue culture cells.

Joshua (1975) reported that the "Lesions are papular, 1mm to 1.5mm in diameter, and may be present as scattered, discrete eruptions or, when numerous and almost as often occurs on the penis, may appear as a moist, granular mass. Individual lesions often appear hemorrhagic with blood oozing from the ulcerated surface; this is most common with penile lesions."

Protozoal Infection

Dourine (Maladie du Coit, Beschälseuche, El Dourine, Exzemansschlag, Lus Venerea Equis, Equine Syphilis, Malignant Venereal Disease of Solipeds). Dourine is due to infection by *Trypanosoma equiperdum.* The disease was first diagnosed in the United States in 1885 by W. L. Williams in DeWitt County, Illinois (Williams, 1888). He remarked that as far as he knew it was the first well-authenticated report of an outbreak of the disease in an English-speaking country. Practically all of the English literature consisted of meager and inaccurate translations from foreign languages. Williams stated that "The earliest account of the disease known is that by the German veterinarian Ammon, who witnessed it in 1796 and 1799 amongst stallions and mares in Trakenen, North Prussia, where it persisted until 1901 and reappeared six years later; but the disease was probably known at a much earlier date in southern Russia." Although several theories have been proposed concerning the entry of the disease into the United States, Williams reported that the most tangible evidence is that it was introduced from France in an infected stallion imported in 1882 into Monticello, Illinois. The horse had been branded on the left side of the crest of the neck with the letters DN, indicating that it had been condemned by the French authorities for maladie du coit.

A description of the gross lesions of dourine in the mare and the stallion was published in the articles by Williams and a summary of the lesions was presented by Hagan (1943). The signs of the disease in the stallion begin with edema of the penis, prepuce, and testes. After the acute lesions in the genital tract have subsided, raised plaques appear on the skin. Hagan stated that "these are frequently called "dollar" plaques because they have the feeling of a disc, like a silver dollar, under the skin. They vary in size from ones much smaller than a silver dollar to ones which are several times as large. These appear quickly and disappear within a few hours or after several days to be replaced by others. At this time depigmentation of the mucosa of the genital tract may occur. Symptoms of paralysis gradually develop, an inconstant fever occurs, emaciation progresses, and death results." I have not seen a description of the histologic lesions that occur in the skin or in the genitalia.

Parasitic Lesions

Cutaneous Habronemiasis (Summer Sores, Swamp Cancer, Bursatti, Esponja). The larvae of *Draschia megastoma, Habronema microstoma, H. muscae,* and various members of the superfamily Filaroidea cause cutaneous lesions in horses (Georgi, 1980). The larvae are transmitted by the common housefly, *Musca domestica,* and the stable fly, *Stomoxys calcitrans.* Parasitic granulomas develop in horses in areas of abraided skin, in the mucosa and skin of the eyelids, and in the mucosa of the penis and prepuce. The penile lesions frequently begin on the urethral process and hemospermia is common when lesions are present in this area. Wheat (1961) stated that the "lesions begin as an inflammatory swelling of the skin, with an intense pruritis which causes the horse to bite or rub the area until it becomes ulcerated. The lesions vary in size and characteristically have an uneven surface which consists of a soft brownish-red material covering a mass of firmer granulations. Chronic lesions sometimes develop into granulomas of considerable size." The lesions are sometimes mistaken for neoplasms on gross examination. The larvae in the granulomas die and the lesions subside during the winter months when the flies are not active. Histologically the lesions consist of granulomas containing numerous eosinophils, parasitic larvae, and tracts through which larvae have migrated. The migration tracts are filled with debris and leukocytes.

Phalloposthitis due to *Strongyloides papillosus.* Beneš and Schanzel (1962) reported the occurrence of acute phalloposthitis in bulls due to infestation by *Strongyloides papillosus.* Numerous larvae were found in preputial washings. The inflammatory lesions disappeared after 1 to 2 weeks and larvae ceased to be demonstrable in preputial washings.

Pediculosis of the Prepuce. Mosaheb *et al.* (1973) reported pediculosis of the bovine prepuce. They stated that "Infestation of bulls with the short-nosed tropical sucking louse, *Haematopinus eurysternus,* usually involved the prepuce and less frequently the scrotum. . . . Macroscopic examination of the prepuce of heavily infested bulls revealed extensive matting of hair around the orifice."

***Cochliomyia hominivorax* Induced Lesions.** The screwworm fly *(Cochliomyia hominivorax)* larvae produce large erosive lesions of the equine prepuce.

Foreign Bodies

Foreign Bodies in the Prepuce and Penis. Johnston (1965a) reported that pieces of straw, plant awns, sharp grass seeds, and urinary calculi may lodge in the preputial cavity of dogs. "The irritation and infection in the preputial cavity are usually mild and often overlooked. There may, however, be a purulent discharge, tinged with blood, and the dog will lick the prepuce frequently." The foreign body may penetrate the tissue surrounding the penis and produce an abscess.

Penile Hypoplasia and Atrophy

The penis remains small and fails to separate from the prepuce in animals that are castrated when young. Penile epithelial crypts, which are androgen dependent, fail to develop in bulls that are castrated as sexually mature young animals and they regress in older bulls following castration. The penile spines of the feline penis are androgen dependent. They develop with increasing age and regress following castration.

Neoplasms of the Penis and Prepuce

Bovine

The virally induced fibropapilloma (fibroma) appears to be the only tumor of the bovine penis. It usually develops in sexually mature young bulls. Jarrett *et al.* (1980) demonstrated that the virus that causes the penile fibropapilloma in bulls is also associated with teat lesions in cows, but is distinct from the bovine cutaneous and alimentary-papilloma viruses.

McEntee (1950) reviewed the literature concerning fibropapillomas of the external genitalia of cattle and reported 28 cases from the vulva and vagina of cows and 27 from the penis of bulls. Desmet *et al.* (1974) reported the occurrence of fibropapillomas in 57 bulls. All the animals but one were less than 3 years of age and the one was 3 years old. Formston (1953) stated that the penile tumors that were diagnosed in bulls less than 15 months of age were very cellular with many mitotic figures and they tended to recur after surgical removal. The age range of 30 cases recorded by Pearson (1972) was 11 months to 3 years 3 months. The tumors were most common in 1- to 2-year-old bulls. He stated that "the most frequent presenting sign is transient haemorrhage after service; the animal may also be reluctant to serve or incapable of normal intromission." Some of the more serious complications included rupture of the penile urethra, penile prolapse and paraphimosis with urine retention, and ischemic necrosis of the tip of the penis.

Some penile tumors of the bull have been misdiagnosed as fibrosarcomas because in the early stages of development they consist of rapidly proliferating fibroblasts with numerous mitotic figures. Fibropapillomas develop in areas of abraded penile mucosa, including the lateral surfaces of the glans penis (Fig. 18.8) and the junction of the penis and prepuce. These are areas that are frequently injured in young bulls during attempted mating. The surface of the tumor is covered by epithelium, which becomes vacuolated (Fig. 18.9) and ulcerated. The developing tumor resembles a fibrosarcoma (Fig. 18.10). As the tumor ages and immunity develops the growth consists of interwoven bundles of fibrocytes with abundant collagenous stromal tissue. If the tumors are removed surgically before immunity develops, they frequently return.

Fig. 18.8. Fibropapilloma on the lateral surface of the glans penis of a 1 1/2-year-old bull. Acc.No. 11008.

Iyengar (1937) reported an epithelioma of the penis of an 8-year-old bull that had phalloposthitis. The histology of the lesion was not illustrated nor described. Thus the diagnosis is questionable.

Equine

The predominant tumors of the equine penis and prepuce are squamous papillomas and squamous cell carcinomas. It is sometimes difficult to differentiate between penile papillomas and carcinomas by examining surgically removed tissue. Squamous cell carci-

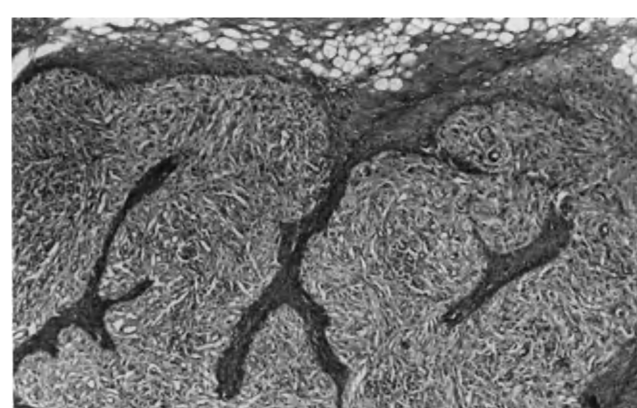

Fig. 18.9. Vacuolated epithelium covering a fibropapilloma of the bovine penis. ×18.5. Acc.No. 4104.

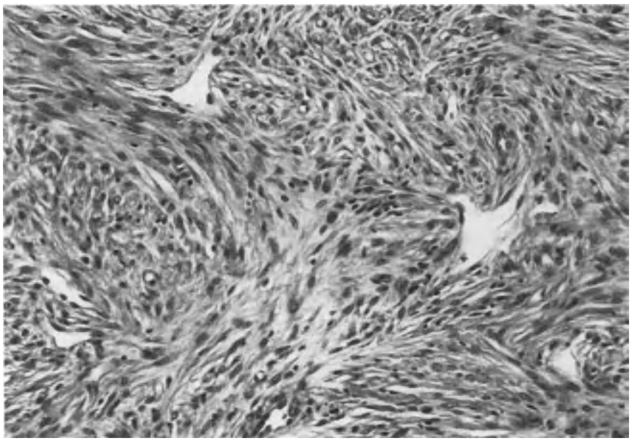

Fig. 18.10. Penile fibropapilloma from a 17-month-old bull. ×178. Acc.No. 14108.

nomas invade regional lymph nodes but are slow to spread to distant sites. These neoplasms occur most frequently in geldings and they tend to start in the nonpigmented areas of the penis and prepuce.

Röder (1926) suggested that smegma plays a role in initiating the start of epithelial tumors of the equine penis and prepuce. Plaut and Kohn-Speyer (1947) demonstrated the carcinogenic action of horse smegma by introducing either whole or a nonsaponified fraction of smegma into an artificially created preputial cavity in mice.

Pires (1944) found penile tumors in 24 of 7998 horses that were examined in Argentina during 1937–1942. There were 22 squamous cell carcinomas, 1 papilloma, and 1 malignant melanoma. Carcinoma of the equine penis and prepuce is of low-grade malignancy but often recurs after amputation and may metastasize (Barrow, 1895; Neefs, 1923; Bräuning, 1928).

Hobday (1892) described a fibroma of the prepuce of an aged pony: "The tumor weighed 3 lbs. 2 1/2 oz., measured 7 1/2 inches in length, and was 15 inches in circumference at its thickest part. It was clearly defined, and surrounded by areolar tissue, the outer surface feeling hard, and being smooth and glistening."

Other neoplasms that have been found on the equine penis and prepuce include sarcoid, lymphoma, lipoma, and hemangioma.

Canine

Transmissible Venereal Tumor (Venereal Granuloma, Infectious Sarcoma, Transmissible Lymphosarcoma, Histiocytoma). The transmissible venereal tumor is the most common penile neoplasm of dogs in certain areas of the world where intact animals are allowed to run free. Ndiritu (1979) reported that in Kenya, 84 of 86 dogs with penile or preputial neoplasms had transmissible venereal tumors. Seventy-eight were on the penis and six on the prepuce. The other tumors were a papilloma and a carcinoma.

Bloom *et al.* (1951) stated that "Under normal circumstances the transmissible venereal tumors are found as single or multiple, small or large, firm, soft or friable, gray to gray-red, sessile or pedunculated, nodular or papillary masses on the penis and at times on the parietal layer of the prepuce. They occur on the glans, sometimes on the entire penis, at the base of the penis and adjacent prepuce, and may extend to the scrotum and perineal region. . . . In both sexes regressive changes are common, so that the tumors may ulcerate and slough, bleed easily, and frequently are associated with a serous, hemorrhagic, or purulent preputial or vaginal discharge."

The tumor cells are uniform in appearance and have large, round, relatively vesicular nuclei that generally contain a prominent, single, eccentrically located nucleolus. There is abundant clear or finely granular cytoplasm. The fibrous tissue stroma is scant but increases in older tumors. Lymphocytes, macrophages, eosinophils, and mast cells are scattered throughout the tumor. Neutrophils are usually present in regressing tumors. A few tumors spread to the regional lymph nodes and some of these metastasize to internal organs.

Other Neoplasms of the Canine Penis and Prepuce. Bloom (1954) reported the occurrence of the following neoplasms on the penis and prepuce of the dog: papilloma, hemangioma, fibroma, sebaceous gland adenoma, circumanal gland tumor, lymphangioma, mast cell tumor (Fig. 18.11), benign and malignant round cell tumors, hemangioendothelioma, fibrosarcoma, reticulum cell sarcoma, and squamous cell carcinoma. Other canine penile and preputial neoplasms include lipoma, liposarcoma, benign and malignant melanomas, and mammary gland neoplasms.

Fig. 18.11. Mast cell tumors of the penis and prepuce of a dog. Acc.No. 15239.

I have not seen neoplasms of the penis or prepuce in the goat, ram, or cat.

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